Acta Genetica et Statistica Medica

Vol. I 1949 Fasc. 3

Index

BASEL (Switzerland) S. KARGER NEW YORK

Printed in Switzerland

The „*Acta Genetica et Statistica Medica*“ is issued quarterly. Each issue has approximately 96 pages. The annual subscription rate is Swiss frs. 44.—.

No payment is made for contributions, but 50 reprints of the article will be sent to the author free of charge. Extracopies, if desired, will be supplied at a special rate. The cost of the engravings will be borne by the publishers, provided the figures and graphs are suitable for reproduction and do not exceed a reasonable number. Otherwise the author after due notification, will be charged with the additional cost. Articles will be printed in English, French, and German, with summaries of about 10 lines. As a rule only original papers can be accepted.

All manuscripts and reviewer's copies should be addressed to *Gunnar Dahlberg*, State Institute of Human Genetics and Race Biology, Uppsala (Sweden). Corrected proofs, however, as well as enquiries concerning subscriptions and notices, should be sent to the publishers, *S. Karger Ltd.*, Holbeinstrasse 22, Basle (Switzerland).

Les „*Acta Genetica et Statistica Medica*“ paraissent en fascicules trimestriels d'environ 96 pages. Le prix de l'abonnement annuel est de frs. suisses 44.—.

Les collaborateurs reçoivent à titre d'honoraires pour leurs travaux originaux 50 tirages à part gratuits. Les tirages à part supplémentaires seront facturés à un prix modéré. La maison d'Edition se charge des frais de clichés à condition qu'elle reçoive des originaux se prêtant à la reproduction et dont le nombre ne dépasse pas la mesure strictement nécessaire. Autrement les frais supplémentaires seront, après avertissement, à la charge de l'auteur. Les travaux pourront être rédigés en langue anglaise, française ou allemande et doivent être suivis d'un court résumé d'environ 10 lignes. Ne seront acceptés en principe que des travaux originaux inédits.

Tous les manuscrits et ouvrages à analyser sont à adresser au Prof. Dr. *Gunnar Dahlberg*, State Institute of Human Genetics and Race Biology, Uppsala (Suède). Les épreuves corrigées, de même que toute correspondance concernant les abonnements et la publicité sont à adresser à *S. Karger S. A.*, Editeurs, Holbeinstrasse 22, Bâle (Suisse).

Die „*Acta Genetica et Statistica Medica*“ erscheinen vierteljährlich in Heften von etwa 96 Seiten zum Jahresabonnementspreis von Schweiz-.Fr. 44.—.

Mitarbeiter erhalten für ihre Originalarbeiten an Stelle eines Honorars 50 Sonderdrucke kostenfrei; weitere Separata gegen mäßige Berechnung. Die Kosten der Clichés übernimmt der Verlag, soweit reproduktionsfähige Vorlagen geliefert werden und die Zahl der Abbildungen das notwendige Maß nicht überschreitet. Andernfalls gehen die Mehrkosten zu Lasten des Autors und werden vorher mitgeteilt. Die Arbeiten können in englischer, französischer oder deutscher Sprache eingereicht werden und sind mit einer kurzen, etwa zehnzeiligen Zusammenfassung zu versehen. Es werden grundsätzlich nur unveröffentlichte Originalarbeiten angenommen.

Alle Manuskripte und Rezensionsexemplare sind zu richten an Prof. Dr. *Gunnar Dahlberg*, State Institute of Human Genetics and Race Biology, Uppsala (Schweden). Korrigierte Fahnen, sowie Zuschriften, Abonnemente und Inserate betreffend, sind an den Verlag *S. Karger A. G.*, Holbeinstrasse 22, Basel (Schweiz) zu senden.

THE THYMUS AND OBESITY

by GUNNAR DAHLBERG

Part 1. Discussion of a theory

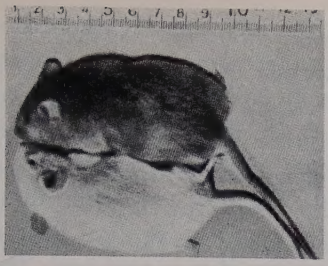
The Appetite.

An adult in equilibrium with respect to his weight must utilize as much as he eats (resorbs) and in the long run neither save of what he eats nor use up more. This is contrary to his strong belief that the amount he eats is more or less decided at random. But if his average food intake slightly exceeded his consumption he would gradually put on considerable weight, and vice versa. If his daily overconsumption is put at, say, 15 g. his yearly weight increase would amount to 5½ kg. A calamity of this sort must be prevented by some mechanism regulating the appetite – overeating must be compensated by a loss of appetite. For it is improbable that the degree of resorption is proportional to the need of the body. The chief regulators of the appetite must be the nervous system and the brain. A person with general paralysis with his brain so degenerated that he is in a state of dementia eats everything offered to him and therefore he often becomes very fat. In order to properly regulate the appetite according to need, however, the brain must in turn be influenced. Most simply this could be brought about by the content of nutriments or related substances in the blood. If this content is high, the appetite will be very low; if it is small the appetite will be ravenous. In addition to this basic factor the appetite also depends on psychological elements. If the food is particularly enticing – tasty and pleasant-looking – we eat more than if the opposite is the case. To some extent the appetite is probably a conditioned reflex; when meal times approach a feeling of hunger sets in, etc. Lastly, the repletion of the digestive organs and especially the fullness of the stomach is of some importance. The sense of satisfaction is intimately connected with this latter factor. In this respect, however, different persons probably react differently; one individual has more fixed habits than the other. This reasoning consequently leads to the conclusion that the appetite

is conditioned by 1. psychological elements, 2. the repletion of the stomach, 3. the content of nutriments in the blood, etc.

Here I shall not discuss the large number of investigations dealing with the mechanism of hunger and appetite, nor is there any reason for dealing with the difference between appetite and hunger. I shall remain content with pointing out that the empty ventricle contracts, a phenomenon which is attended by a sensation of hunger (*Cannon* of U.S.A. 1911–12). The physiologist *Carlsson* of Chicago (1916) by reasoning in about the same way as we have done here has come to the conclusion that most likely the blood sugar is the factor which determines the appetite. Therefore he has suggested that insulin treatment should be used to give lean people a better appetite. And, to be sure, such treatment has sometimes been effective. However, later investigations by *Scott*, *Scott* and *Luckhardt* (1938) have shown that there is no relationship between the amount of blood sugar and ventricular contractions. It therefore seems rather doubtful that the hunger should be due to the blood sugar. Nevertheless, *Luckhardt* and *Carlsson* (1914) have demonstrated that injection of blood from a starving dog induces ventricular contractions in normal dogs. These experiments indicate that the state of the blood must be of importance for the appetite. In the blood the substance of importance is probably not the glucose it contains. It does, however, seem plausible that the decisive factor is to what extent nutriments are mobilized from the tissues to the blood. When the body begins to reach the end of its reserves of for instance glycogen a special substance might be secreted which causes hunger. This would explain why there is no parallelism between the amount of blood sugar and a sensation of hunger. Such being the case the important thing would be if the nutriments in the blood came from the reserve of the organism or from the food. But it is not necessary for our purpose to take up a position pro or contra this question, and that is why I have confined myself to speak of nutriments in the blood or related substances. Anyhow, in the following it matters little whatever the case may be. For the sake of brevity I shall in the following often talk only of the amount of nutriments in the blood.

Before passing on it must be mentioned that *Weitze* (1940) in her important studies of obesity in mice carried out parabiotic experiments between fat and lean mice. If an effective blood exchange between the animals was established they attained the same weight; otherwise their weights became very different. This cannot be due to a



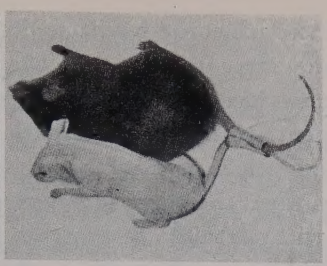


Fig. 1. *Fig. 2.*

Fig. 1. Parabiosis between an originally lean mouse and a fat mouse (the dark animal). Effective blood exchange between the animals was established and they subsequently attained about the same weight. After *Marie Weitze.* *Fig. 2.* Parabiosis between a lean mouse and a fat one. Tests when methylene-blue was injected showed that no blood exchange had been established. The animals remained of different weights. After *Marie Weitze.*

different tendency of the tissues in the animals to store up food-substances. Consequently these experiments also show that the quality of the blood is of decisive importance. Like many other authors *Weitze* suspects some pituitary hormone, but she does not seem to have thought of the thymus. In regard to the pituitary gland she found no difference, however. Nor was there any significant difference between the blood sugar of fat and of lean mice. The difference amounted to 0.005 ± 0.006.

The blood and tissues in fat and lean persons.

The nutriments present in the blood may be used up or be assimilated by the tissues and stored. Probably the cells have a varying capacity of acquiring nutriments from the blood. In this respect the adipose tissues have a special talent. If they absorb the nutriments the person concerned sooner arrives at a point where he must mobilize nutriments in order to maintain their content in the blood on a normal level. A great storing capacity can be the cause of a large appetite.

The function of the thymus.

We know next to nothing of the function of the thymus. On the other hand we do know that normally it remains comparatively large until puberty and then gradually decreases considerably. We also know that in a starving person it decreases very rapidly and that it

regenerates when the nutritional state improves. It also decreases in pregnancy after which it once again increases. Owing to its structure the thymus has been assumed to be an endocrine gland, but ordinary experiments to demonstrate such function have failed utterly. Different investigators have given very divergent reports as to what happens when the gland is removed. The only conclusion that can be drawn with certainty is that the thymus has no vital function and that nothing very dramatic need happen if it is removed. The latest "discovery" concerning the function of the thymus is that it has something to do with the metabolism of sugar (*Bomskov*), but this has not been confirmed. Some authors have maintained that the thymus is of importance in the neutralization of certain toxins but this also is a mere conjecture. Experiments with thymic substance administered perorally or parenterally have not given any decisive results. It is reported, however, that such administration promotes the growth of rats (*Ascher* 1936). It has also been found that the thymus is especially large in patients suffering from Basedow's disease, i. e. in those who die during or following an operation without being cachectic. The much discussed fatalities with hyperplasia of the thymus which seem to be without adequate reason are similar to these deaths after Basedowian operations. As a concept the thymico-lymphatic status has been much debated and no agreement has been reached. That the thymus and the thyroid gland are antagonists has been generally accepted. It has also been found that adolescents with a large thymus have undeveloped reproductive organs, and this might indicate some sort of antagonism between the thymus and the sexual organs. For certain reasons it may be assumed that the suprarenal glands influence the thymus. Of late the phenomenon called stress, i. e. both physical and psychical strain, has been especially in the limelight. The reason for this interest is that stress is attended by certain changes in the endocrine organs and the activity of the suprarenals increases whereas the thymus on the contrary becomes atrophied. These changes are looked upon as a kind of preparedness for an emergency.

The endocrine organs as well as the genes are like the instruments in an orchestra; they are in harmony or discord. In a manner of speaking it is meaningless to ask for the specific function of an endocrine organ, just as it is of a separate gene. The only thing that can be determined is the difference when the organ is present and when it is absent. The position would be more or less the same if the sound of a

certain instrument could be determined only by listening to the orchestra with and without the instrument.

Actually quite a lot is known about the thymus but its function is not really known. Such being the case there is every reason to try to deduce something from what already is known. The first thing that comes to mind is the particularly interesting fact that the thymus reacts so rapidly to undernourishment. No other organ does so as quickly or as markedly. If we suppose that the thymus has an endocrine activity (an account of the thymus is included in practically every textbook and manual on endocrinology), then an absent thymic function should make itself especially felt in a state of undernourishment. When the diet is deficient, it becomes necessary to mobilize the reserves of nutriment of the body, fats especially, in order to maintain the combustion on an adequate level. Starvation is attended by a slightly subnormal blood sugar level. Initially sugar is mobilized from the glycogen depôts, but after some days the depôts of fat begin to be drawn upon. During starvation sugar may also be formed from proteins. Consequently a disappearance of the thymus should facilitate these processes, provided that the disappearance has some purpose and not is due only to a strange susceptibility with no real object[1]). If the disappearance of the thymus facilitates the mobilization of nutriments, a well developed thymus should have the opposite effect, i. e. promote storing of nutriments, especially fats, in the tissues. As emphasized previously the nutriments present in the blood may be utilized in two ways: 1. to maintain the combustion, 2. for other purposes. In the latter case there are three plausible possibilities, viz. a) a consumption to render possible a reparation of tissues destroyed by combustion or function, b) consumption to make possible creation of new tissues, especially during growth, and c) storing especially in

[1]) In reality, this essay is nothing but an attempt to solve the thymus problem by straight thinking. I would therefore draw the reader's attention to the fact that here two assumptions are made on which everything that is to follow is based: firstly, that the thymus has an endocrine function, which by no means is certain; and secondly that the reduction of the thymus in inanition bears some relationship to its function, which also is unproved. The fact is that purely logical reasoning only leads to results which are inherent in the assumptions made. If it is desirable to progress further, reasoning by analogy must be resorted to, and such methods are logically unsound. In medical science as in practical healing more or less wild guesses are often made. So as not to be forced to make additional assumptions I have confined myself to a fairly vague formulation of some points of my theory and that is tantamount to saying that there are several possibilities left open.

adipose tissues for future needs, a storage which often is utterly meaningless and tends to become pathological.

Thus, it would appear as though this were the function of the thymus, viz. to stimulate the cells to take up nutriments from the blood stream. Fat cells, particularly, are stimulated in adults, but probably other cells also and especially so during growth. It is simple, consequently, to realize why the thymus is comparatively large during childhood. The fact that the thymus is particularly large during growth may suggest that it has some function in the storage of proteins. In youth saving is necessary for growth and then an organ is needed to stimulate saving. For adults, on the contrary, it is dangerous to save so much. Hence the thymus must be less effective in grown-ups and therefore it is "reasonable" that then the thymus tends to decrease. On the basis of the hypothesis just presented the "antagonism" between the suprarenal glands and the thymus seems more natural. An increased secretion from the suprarenal glands raises the blood sugar level by a mobilization of glycogen. The state of preparedness for an emergency should not be counteracted by the thymus. Therefore it seems natural that the thymus then diminishes.

The behaviour of the thymus during pregnancy is not quite so easy to reconcile with the above hypothesis. At such times women also need to save up nourishment. But the important thing is that they do not have to save for themselves but on behalf of the fetus. Therefore the thymus in pregnant women is small so that the content of nutriments in the blood becomes high. This is in fact essential for the growth of the fetus. To what extent the thymus in the fetus is capable of influencing the mother at the end of the pregnancy is of course an open question. In any case I should think that the behaviour of the thymus is not the same in all women, that in some the thymus decreases but little or not at all and therefore the mothers grow fat at the same time as the fetus develops. When the fetus abstracts nutriments from the blood of the mother the appetite sharpens and the result is an increased supply of nourishment. Consequently the blood will be very variable – sometimes its content of nutriments will be high, sometimes low. At times the result of this is that the mother also fattens and probably this takes place especially when the size of the thymus does not go down much.

It is only natural that the thymus should be an antagonist to the thyroid gland if the theory presented here is correct. In hyperthyroidism the consumption increases. To ensure that an adequate

proportion of the nutriments in the blood are saved for repairs and the like the thymus must in this condition increase its function and stimulate the cells to absorb more readily. Then a situation arises when the nutritive substances in the blood stream vanish comparatively rapidly. It is not strange that such persons are particularly taxed by large operations. They have very few mobilizable reserve nutriments as long as both the thyroid gland and the thymus function excessively, i. e. as long as these persons suffer from both hyperthyroidism and hyperthymia simultaneously. When such people are operated upon their supply of food will for obvious reasons be on the short side for a time. This puts them in an especially dangerous situation and explains the formerly rather frequent fatalities. Nowadays administration of iodine or thiourasil preparations is used to render the thyroid function more normal, i. e. the rate of combustion is reduced prior to an operation. By this means the risks have been considerably minimized.

The situation is analogous as regards the much disputed deaths in a thymicolymphatic state. *Hammar* was inclined to deny that such unexpected deaths had anything to do with the thymus. Other and also later authors have, however, all the while spoken about thymic deaths. Without taking up a definite attitude to the matter I wish to point out that it would be strange if no cases of thymic hyperplasia existed, and to me it seems quite conceivable that such hyperplasia may occur, especially when the gland normally is at its height, i. e. during puberty. Owing to their hyperthymia such persons should have blood with only small amounts of available nutriments. An insignificant exertion, a momentary increase in the consumption of energy may then perhaps be very dangerous, particularly some time after a meal. My best guess is that at such times the brain is undernourished and that the person is thrown into a faint which may pass into death.

The negative result of the experimental investigations on the thymus remains to be explained. If the thymus were removed the immediate result should be a reduced appetite and slightly retarded growth. The appetite has been neglected because it is difficult to estimate quantitatively. That the growth often does become retarded has been found, but it has also been observed that if the animals are given plenty of nourishing food and their nutritional status is not impaired the thymusectomy has no effect. In other words, this is exactly what should be expected according to my theory.

Experiments in which thymic substance is administered should, if continued long enough with adequate doses, actually containing the active compounds (which by no means is certain), entail that the test animals gradually became fatter, provided that they could eat at their heart's delight. If, on the contrary, the diet were restricted to normal requirements, there would be no fattening and no effect whatsoever. The meagre results of the experiments are in other words more or less in line with the author's hypothesis.

It now remains to be explained why the sexual glands are inhibited by a large thymus. To me the problem seems to be rather intricate. It may be assumed, however, that if the individual is retarded in the development, if, for instance, in this respect there is a repression conditioned by special genes, the result will be both a large, persistent thymus and a continuation of the sexual glands in an infantile stage of development. If such is the case, there need be no true antagonism. However, a true antagonism might actually exist. This is indicated by certain experiments. It would also from a certain point of view be fairly natural. In any case the function of the thymus decreases when the activity of the sexual glands commences.

The problem of obesity.

In modern times the only persons who doubt the law of the conservation of energy are excessively fat people. Almost as regularly as clockwork they assure anybody who cares to listen that they eat no more than other people and yet they grow fat. One reason why they say so is that they put on weight even if they do not eat until they are satiated and consequently curb their appetite to a higher degree than ordinary people. For, according to the theory outlined in this paper, the decisive factor for their obesity is that they have an abnormally large and efficacious thymic gland which causes them to store abnormal reserves of food, even if the content of nutriments in the blood should be no higher than normal. If they eat less than they need, i. e. than the amount corresponding to the normal content of nutriments in the blood, they constantly feel hungry. The fact is that they have a greater appetite than normal persons and that is what causes them most worry. The question is what can be done about it.

The immediate consequence of the hypothesis I have outlined is that in excessive obesity the thymus or the greater portion of it should be extirpated. The operation may not be easy to carry out,

however, although it is simple to perform on animals. The proximity of the thymus to the lungs and the large blood vessels must also be taken into account and this contributes to make the operation a tricky one. Consequently such a step is out of the question except in very severe cases if at all. As before slimming regimentations must be tried first of all. A severe but brief course of restricted diet to near starvation might possibly be attempted. A few days of this and the thymic gland will become smaller and be less effective. When a more normal diet later is resumed the patient will probably have a less strong appetite. If this is moderately satisfied, the appetite should subsequently become more normal. In other words a slimming cure will thenceforth be easier to carry through. It must be remembered, however, that in due course the gland will again grow out and then a new period of starvation may be indicated. This is especially true if the dietary limitations necessary to prevent the thymus from developing cannot be enforced. But this is merely an hypothesis and therefore it is not possible to arrive at any conclusions as to how long the starvation period should be and how severely restricted the diet should be thereafter. It is also possible that in fat people the thymus gland is especially resistant to fasting. Lastly, it should be mentioned that since the starvation during the first days surely must be very difficult to endure – otherwise it would hardly be effective – it might be justifiable to use special therapeutical means to mollify the hardships attending the fasting. d-Phenopromin (Afatin) may become very useful if it comes up to promises. Naturally sedatives of various kinds and other symptomatics could also be used to soothe the discomforts of a short period of starvation. It may be mentioned that some narcotics have a very marked effect on the thymus and therefore may be useful during this period. The dangers entailed by the inadequate supply of food in hyperthymia must of course not be disregarded. Untoward effects and hasards may be feared because the blood to an excessive degree is deprived of its nutriments. Here it should be remembered what previously was said when discussing the so-called thymicolymphatic state. Actually the voracious appetite of fat people is a protection against inanition which prevents them from starving to death despite their superabundance. The attitude here presented sheds some new light upon the hasards associated with a slimming cure.

A final possibility that might be resorted to is X-ray treatment of the thymus. A priori it is difficult to say how effective such therapy would turn out to be. It is known, however, that in animal experi-

ments the thymus has proved to be very susceptible to such irradiation. Probably the best effect would be attained by combining a slimming cure with X-ray treatment. It might perhaps be most suitable to commence the slimming cure about a week after the X-ray treatment and then begin with a period of starvation. After the starvation period a suitable diet, not too rich in calories, should be prescribed.

The not uncommon method of combining a slimming cure with thyroid treatment or of using thyroid treatment only should, however, suffer from some drawbacks. In hyperthyroidism the thymic gland sometimes increases in size. However, the enlarged thymic gland would cause easily formed adiposity after the end of the cure, particularly if the slimming cure had been comparatively moderate and therefore without effect on the thymus. It is worth emphasizing, moreover, that the situation arising as a cause of simultaneous thyroid therapy and, possibly, enlargement of the thymus should be especially difficult to stand up to. For the combustion increases at the same time as the storing of nutriments in the tissues goes up. This should cause a relatively great deficiency of nutriments in the blood.

Finally it should be kept in mind that after an intensive slimming cure some cases of obesity do not again become fat, whereas they on the contrary tend to emaciate. If my theory is correct this would be due to a degeneration of the thymus owing to the intensive slimming not followed by regeneration of the gland. It should be mentioned that the treatment recommended here (combined X-ray irradiation and slimming cure) should be especially efficacious when applied to young and middle-aged persons. On the contrary it probably would not be so well adapted for old or very old individuals.

The problem of lean people and the lack of appetite.

According to the hypothesis given in this paper a disposition to extreme leanness is due to an ineffective thymus, which implies that the tissues are not stimulated to absorb more food than absolutely necessary from the blood. In other words all the food is used up for combustion and possibly growth. If by chance the supply of nourishment should at some time be deficient the reserves in the fatty tissues will be drawn upon and the former will then be poorly refilled. The natural consequence will be that the person concerned becomes extremely lean and almost emaciated. From the above discussion it is evident that his appetite should be rather low in comparison to his

consumption of energy, or more correctly, that the craving for food relatively soon passes away. Naturally, leanness may also have psychological reasons, but if the person concerned just picks at his food the thymus will degenerate until it practically vanishes and then the appetite becomes even lower. The extreme emaciation associated with Simmond's disease is ascribed to changes in the hypophysial function. As far as I know, nobody has investigated whether this in turn is attended by a change in thymic function.

Those who professionally deal with starvation, so-called hunger-artists (fakirs), are able to remain without food with comparative ease since by their training in starving their thymus has disappeared or been reduced to a minimum. From psychological points of view lean persons can naturally sustain hunger more easily than fat people, although the latter in the long run perhaps do better because they have a reserve store to draw upon.

When ordinary persons who have not trained themselves to starve are forced to manage without food or get only very little, e. g. prisoners in concentration camps and similar unfortunates, the sensation of hunger can be expected to be especially trying psychologically during the first week, and the pangs of hunger tax the fat ones most. For the latter the second week should be better because by this time the thymic gland will have had time to degenerate and become less effective. Gradually the thymus should atrophy altogether and then they sustain starvation without too much trouble. They finally get into a stage of extreme inanition without any appetite worth mentioning and become the counterparts of the "mussel men" in the German concentration camps during the second world war. Owing to the low content of nutriments in the blood the brain functions very badly and they therefore become indolent and do not react normally to impressions.

If we return to discuss the lean persons it is obvious that their lack of nutritional reserves must cause some discomfort. The emaciated ones especially may, if they have to go without food for a short time only, soon get into a similar condition as very fat people. Lean persons also get a deficiency of nutriments in the blood comparatively easily and this should cause troubles like weakness and susceptibility to fainting, etc. The troubles probably become severe or lead to death in exceptional cases only. A small proportion of the deaths assumed to be due to orthostatic anemia, however, may have hunger as a contributory cause. In any case it must be the lack of reserves, causing

the content of nutriments in the blood to easily drop below par, which contributes to the danger of the circulatory disorder. The lean starve to death in their poverty because they have no capital to tide them over a hard time.[1])

When leanness is to be treated thymic substance or thymic hormone should of course be administered. Unfortunately, the latter substance has not yet been discovered but perhaps it will be the therapy of the future. At present all that can be done is to fatten the person concerned. A fattening course rationally carried out necessitates that food should be administered as soon as the stomach is empty. In other words, the less accentuated sensation of hunger which is due to an empty stomach should be made use of. Besides, it would seem as though a bout of short but strenuous excercise shortly before meals were a rational measure. By means of a momentary increase of the combustion the appetite will be increased and it then becomes easier for the person concerned to take food.

Seemingly my theory is contradicted by the fact that diabetics who do not get insulin treatment have a voracious appetite, although they have an increased content of glucose in the blood. It is characteristic of the disease, however, that patients cannot utilize and consume their sugar to the normal extent. It behaves rather like a substance which is more or less indifferent to the body. In so far as this causes a high level of blood sugar, sugar must be mobilized from the glycogen depôts. This causes an increased appetite. Nowadays, however, insulin has been discovered and the problem is rather different. The fact that insulin can be used to improve the appetite of non-diabetics is due to the very circumstance that the appetite increases when the blood sugar is low, because then sugar also must be mobilized from the glycogen depôts.

The treatment of obesity outlined in the above is especially valid for obesity suspected to be due to thymic hyperplasia. Fatness which

---

[1]) I have previously pointed out that both excessively fat and excessively lean individuals are especially sensitive to physical exhaustion, particularly if they have received insufficient food. As a rule they have to starve for some time before an operation. Before that they may have been unable to eat adequately. To me it is therefore by no means unexpected that there are occasional, apparently unexplainable deaths during and after operations. In order to combat this outcome it might be a good idea to give an injection of glucose or a solution of amino-acid before an operation, and possibly after it also, i. e. in cases when the patients are especially lean or fat and the operation is a severe one.

simply is due to overeating, e. g. in some children, and which is not attended by thymic hyperplasia should have rather different characteristics and should hardly attain such excessive forms.

In analyzing the causes of obesity it is usual to start with the psychological side of the picture. Often that is as far as one gets. In the United States, especially, it has become the vogue to construct psychological backgrounds for obesity and, sure enough, European imitators have sprung up.

It might be a good idea to look at the other side of the question and commence with obesity from the angle of the adipose tissue. Obviously the adipose tissue absorbs more nutrition in fat persons than in lean ones. But this cannot be due to intrinsic differences in the tissues – a fact proved by the parabiotic experiments by *Weitze* mentioned in the foregoing. If the tissues get the same blood, they will absorb about the same amounts of fat. The reason why fat persons' adipose tissue stores up more reserve nourishment than lean persons' might be that the blood of the former contains more nourisment than that of the latter. But strangely enough no differences have been observed in the blood sugar contents in fat and lean people. We would again emphasize that fat and lean mice apparently do not differ significantly as regards blood sugar content. Naturally, however, the blood in a fat person must in the long run convey more nourishment than in a lean. Otherwise no reserves could be stored up. The difference in the content of nutriments in the blood is so insignificant, however, that it cannot be determined, at least not as regards blood sugar. One reason why there is no difference in the content of nutriments of the blood may be that the tissues rapidly absorb any surplus, thereby preventing an increase. In other words, there is a more rapid turn-over in the blood of fat people. That is what my hypothesis finally amounts to. If the adipose tissue in the fat person absorbs too much he runs the risk that his blood will become deficient in nutriments. When the content falls below a certain value, nutriments must consequently be mobilized from the tissues. Such mobilization might be attended by secretion into the blood of an "appetite promotor". The mobilization is necessary much earlier in fat than in lean persons. Therefore the fat person will have a more hearty appetite. If the fat person does not have a greater appetite and yet eats a lot and his adipose tissue functions normally his blood sugar ought to increase. This increase, if any, should be measurable when the obesity is due to overeating and not to a personal predisposition.

From this reasoning it follows that the blood sugar in fat and lean persons ought to be more systematically studied, especially after tolerance tests and so far as possible on comparable dietic terms. Naturally no pronounced differences are to be expected. If so, they would have been known long ago. The differences, if any, can only be discovered by statistical analysis of a large number of cases. Besides, it is obvious that these differences must be small. In the long run, their effect will still be considerable. There should be differences not so much between fat and lean persons as between those who are in the process of becoming fat or lean, respectively.

The thymus in normal persons.

In normal persons the thymic and thyroid glands are in equilibrium. Naturally this state of balance may vary so that in some the thymus is slightly predominant and in others the thyroid gland is a little ahead. From this point of view it would be correct to speak of thymus excessive and thyroid excessive persons. The former are a bit on the round side while the latter are rather angular. Actually the constitutional types probably conform rather well with this grouping. Lean and frail persons, by *Kretschmer* called leptosomes and by *Sheldon* assumed to be more ectomorph, and the athletic type (*Kretschmer*) and the mesomorph type (*Sheldon*), who also are lean but have well developed skeletons and, chiefly, muscles, both probably are what I would call thyroid excessive. Persons who are fat but not abnormally so and who *Kretschmer* calls pycnic and *Sheldon* especially endomorph, probably represent the thymus excessive type according to my terminology. However, these labels possibly imply a dangerous simplification. Elsewhere (*Dahlberg*, 1949) I have criticized the tendency to use these types with no defined boundaries when we really have to do with continuous variation. In this connection I merely wish to stress the point that in part these popular types may be based on what amounts to nothing but a variability due to the endocrine organs, chiefly the thymus and the thyroid gland.

Obesity and aging.

During early fetal life there is no thymus. Then the cells absorb nourishment without special stimulation. The thymus develops to perceivable size only during the third and fourth fetal month and towards full-term it is comparatively large. It may naturally be as-

sumed that during this process the importance of the thymus increases steadily and that its stimulating effect on the absorption of nourishment by the body cells becomes more and more significant. It may be asked what happens if the thymus does not develop, i. e. if we have a case of thymic aplasia. Such cases have not been observed, however, and late fetal growth is probably impossible without the thymus. The fetus probably dies and the pregnancy results in an abortion. The thymus is not vital to adults. During late fetal life and in early childhood perhaps it is. Children with a small and fairly ineffective thymus are of course difficult to nourish. It may also be supposed that children who despite being born at full-term refuse their food and do not gain weight may have an ineffective thymus. It is not out of the question that some time in the future they will be treated with thymic hormone. Children whose thymus is overactive will by the same token easily become overfed. Thereafter the thymus is particularly active up to puberty after which it becomes slightly less effective, which has been discussed in detail in the foregoing. Old people sometimes acquire a tendency to grow fat. This is especially true of women in the menopause whereas for men it is impossible to fix the time so definitely but probably their obesity as a rule starts somewhat later. As mentioned earlier the fact that women tend to put on fat in the climacterium possibly is due to the antagonism between the sexual glands and the thymus. As soon as the sexual glands cease to function the thymus becomes predominant. Therefore the appetite increases and the person concerned tends to become obese. Men may have the same mechanism but in them it cannot be determined when the sexual glands cease to function. If a man of, say, 50, starts to grow fat it may in other words be surmised that his sexual activity is declining. When people grow middle-aged and old it is probable that the changes in the thymus exhibit great variability. Sometimes it atrophies, sometimes it increases, and this could be one of the reasons why some oldsters become very fat and others very skinny.

On the whole our discussion of the problems has been rather schematic. The person who becomes fat probably has an abnormally effective thymus. In so far as obesity is hereditary it is likely that the characteristics of the thymus are hereditary. But the thymus is only one side of the question. For it might also be that the tissues respond differently to the secretion of the thymus. It is hard to say anything definite on this point. What can be said, however, is that

adipose tissues in various parts of the body respond differently to stimulation. In some women the upper parts of the body tend to become fat, in others the lower parts. Most of them seem to grow fat all over. This may be because the fat in the respective parts of the body is more responsive to thymic hormone than that in other parts. However it is rather dubious for how long the thymus may be important. As emphasized before, it is probably most important in young people up to 30 years of age.

Therefore old people probably come in a group by themselves. Often their facial adipose tissue does not absorb so much fat. In most old people the skin of the abdomen on the other hand seems to have a very marked tendency to take up fat. This circumstance is beautifully illustrated by a case of skin grafting performed in Sweden when the method was new (*Strandberg*, 1915). The skin on the dorsal part of the hand (which had been destroyed) was to be replaced by skin from the abdomen. Owing to the imperfect technique of the day some of the abdominal fat happened to be transplanted along with the piece of skin. This did not cause any trouble, however, and everything was fine. But when the woman entered the climacterium and began to grow fat, both her abdomen and the back of her hand grew fat. At the latter site the adipose tissue bulged out in the form of a bun. In old people the abdominal tissue is evidently especially liable to proliferate and absorb fat. It appears as though this tendency might be common to some connective tissues. I would remind the reader that some old people have a proliferative tendency in the connective tissue of the intima. It has been said that arteriosclerosis commences espe-

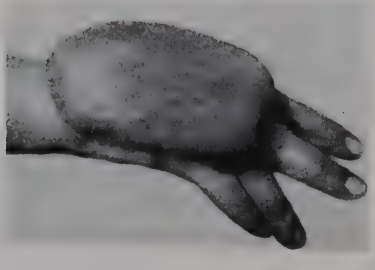


Fig. 3. Transplantation of skin from the abdomen to the dorsal part of the hand. The figure shows the appearance of the hand, when the person in question became older and fatter. After *Strandberg*.

cially early in fat people and that they get it very badly. It is not certain, however, that this is so. To my knowledge no conclusive proofs have been presented and the attitude is solely based on so called clinical findings. However, if there should turn out to be a relationship of this kind it could for the present best be expressed in the above form.

The thymus and salmon-fishing.

What the hypothesis presented here boils down to is that the thymus controls the investments in the planned economy of the body. On several points this hypothesis has proved to fit in with what is known. As a matter of fact I almost succeeded in convincing myself, when I dictated this, that my theory might be true. I feel tempted to travesty Voltaire and say that if the thymus does not have the properties it ought to have according to my theory another organ that has them must be looked for. It has of course been tempting to formulate the hypothesis more in detail and it also would be enticing to discuss it from general biological aspects, e. g. with reference to hibernating animals and to migratory birds etc. I have, for example, not discussed the various components of the gland and their importance in different situations, and, furthermore, only in passing have I touched upon the relationship between the thymus and other endocrine glands. Lastly, I have not discussed the role of the thymus in myasthenia gravis[1]). Here I merely wish to stress that very probably the thymus has several functions and therefore the hypothesis made should not be pressed too hard. Consequently I shall refrain from discussing these problems and permit myself to digress on one point only.

With respect to salmon-fishing it is a known fact that when the fish attain a certain age their sexual organs begin to function. Compelled by the awakened sexual urge they ascend the rivers from the sea in order to spawn. In connection with the increased activity of the reproductive organs it may be supposed that the size of the thymus diminishes and that the gland perhaps disappears completely. Therefore they eat nothing during the spawning season. In time they

[1]) The rapid exhaustibility associated with myasthenia gravis is most easily understood if it is assumed that the reserves are inadequate of some substance which is essential for neuromuscular activity. If so, thymic hypertrophy might perhaps be a compensatory reaction to stimulate the saving of the critical substance. Therefore no effect of X-ray treatment of the thymus should be expected. Nor has an effect with certainty been obtained. I merely wish to point out that there are two possibilities and that it cannot at present be determined which one is correct.

become emaciated and indolent, rather like the "mussel men" of the concentration camps, after which they drift in an almost helpless condition to the sea where they die, if not sooner, because of lacking appetite. This applies to the Alaskan salmon. The species of salmon we have in Sweden is similarly affected but not so markedly. Therefore our salmon "winds somewhere safe to sea" and is thought capable of repeated spawning jaunts later. If people who catch salmon for sport made a habit of saving the heads for scientific study their strange pastime would be of some use.

It is remarkable that the thymus is encountered so low in the animal world. This indicates that it has at least one function which is of basic importance. On the other hand the thymus may have many functions. This is not the place, however, to discuss that side of the question.

Future thymus research.

In the above we have endeavoured to explain why experimental thymus research has yielded so contradictory and on the whole negative results. Possibly it will be feasible in the light of my theory to perform experiments so planned that they really give results. In order not to quell the desire of other scientists to check this theory of mine, I shall not tell how I think the experiments should be carried out. After all, it should primarily be determined whether the thymus has the effect I have attributed to it. Only in the second place, when one knows that there is something to look for, does one have to face the problem of isolating the hormone or hormones responsible for the thymic effect.

What otherwise should be of especial interest would be to determine the changes in the thymus in excessively lean and excessively fat persons, respectively. It is a fact, which repeatedly has been mentioned, that the thymus rapidly diminishes in volume during inanition. Most people who die in disease are in such a state, or more correctly, owing to their disease they are unable to eat at all enough during the days immediately preceding death. Therefore the thymus becomes small in fat persons too before they die and at autopsy no very marked difference has been observed in fat and lean individuals. In order to get a correct idea of the size of the thymus one must, as emphasized by *Hammar*, confine oneself to a study of persons who have died on account of suicide, accidents or the like. It should not be difficult, however, to carry out such an investigation of fat and lean persons in this era of motorized locomotion and global warfare.

Hypotheses and science.

I usually maintain that one important difference between scientific thinking and ordinary thinking is nothing but a deep mistrust of the faculty of straight thinking. Even a simple thought-process like addition cannot be performed for any long time without making mistakes. Indeed, in the long run errors will certainly be made. Checking is therefore necessary and the proper way to set about scientific work is to think for a long or a short time and then by experiments or otherwise control the validity of the thoughts. Indeed, scientific works are rarely if at all published without such more or less conclusive controls. Works based on pure thinking which have not been verified in any way are usually not published.

A few words are needed to explain why I have not adhered to this custom now. First of all the problems in question have been debated for several hundred years without tangible results, not even a plausible hypothesis. This makes it more justifiable than usually is the case to publish a purely hypothetical work. Another reason is that it is difficult to check these matters. Experimental proof is not readily obtained. Besides, I am in a position which makes it particularly difficult for me to arrange for such matters, all the more so as the problem is rather outside my province.

When as in this case we are dealing with a hypothesis that connects so many known phenomena which otherwise would stand isolated, this very fact is a sort of verification, at least sufficiently so to justify publication.

In closing I shall merely emphasize that most of the suggestions made in this paper are comparatively harmless. However, if my recommendations are followed I wish to stress that all I have done is to advance a hypothesis with the sole object of stimulating to continued research. My suggestions are far too vaguely substantiated for me to shoulder any responsibility for them. However, I am now trying to get more conclusive proof of my hypothesis.

Summary.

Firstly what we know about the cause of hunger and appetite is discussed. It is shown that according to our present knowledge the decisive factor seems to be the content of nutriments in the blood coming from the reserves in the body, not directly from the food. Fatness depends on a tendency to store nutriments in the adipose tissue. Then the function of the thymus is discussed and it is shown

that according to our present knowledge it seems reasonable to assume that this tendency to store nutriments is regulated by some special substance coming from the thymus. A new form of treatment for young people especially is then proposed.

Résumé

En premier lieu, l'auteur discute ce que nous savons des causes de la faim et de l'appétit. Il montre que le facteur décisif, au vu de nos connaissances actuelles semble être le contenu en aliments se trouvant dans le sang provenant des réserves de l'organisme, et non directement de la nourriture. L'obésité est due à une tendance à accumuler les aliments dans le tissu adipeux. La fonction du thymus est alors envisagée et l'auteur montre que dans l'état actuel de nos connaissances, cette tendance à mettre en réserve les aliments est sous la dépendance d'une substance spéciale provenant du thymus. Il propose ensuite une nouvelle forme de traitement convenant particulièrement aux personnes jeunes.

Zusammenfassung

Zunächst wird das, was wir über den Grund von Hunger und Appetit wissen, besprochen. Es wird gezeigt, daß, unserem heutigen Wissen entsprechend, der entscheidende Faktor der Gehalt an Nahrung im Blut zu sein scheint, der von den Reserven im Körper kommt und nicht direkt aus der Nahrung. Fettsucht beruht auf Neigung, die Nahrung in den Geweben zu speichern. Außerdem wird die Funktion des Thymus besprochen und gezeigt, daß, abermals gemäß dem heutigen Stand der Wissenschaft, es glaubwürdig zu sein scheint, anzunehmen, daß die Tendenz Nahrung zu speichern durch eine besondere Substanz, die vom Thymus kommt, reguliert wird. Eine neue Behandlungsform besonders für junge Menschen wird vorgeschlagen. Im zweiten Teil der Arbeit wird die hier aufgestellte Theorie so weit als möglich geprüft werden.

LITERATURE CITED.

Asher, L.: Physiologie der inneren Sekretion. Leipzig und Wien, 1936. – *Cannon, W. B.* and *A. I. Washburn:* Amer. Journ. Physiol., Vol. 29, 1911–12. – *Carlsson, A. J.:* The control of hunger in health and disease. Chicago 1916. – *Luckhardt, A. B.* and *A. J. Carlsson:* Amer. Journ. Physiol., Vol. 36, 1914. – *Scott, W. W., Scott, C. C.* and *A. B. Luckhardt:* Amer. Journ. Physiol., Vol. 123, 1938. – *Weitze, M.:* Hereditary adiposity in mice. Copenhagen 1940.

BEITRAG ZUR KENNTNIS DER DYSOSTOSIS MANDIBULOFACIALIS UND IHRER ONTOGENESE

Übersicht der bisher in den Niederlanden beobachteten Fälle

von P. J. WAARDENBURG und H. NAVIS (Arnhem)
Augenarzt Ohrenarzt

Im Jahre 1932 hat der eine von uns das Krankheitsbild eines von ihm 1930 beobachteten Falles beschrieben. Es handelte sich um einen 7jährigen Knaben mit Lidspalten-, Wimpern-, Jochbein-, Unterkiefer- und Ohrenabnormitäten, die auf eine angeborene Entwicklungsstörung deuteten. Auf der 84. Tagung der Niederl. Ophth. Ges. wurden stereoskopische Frontal- und Profilaufnahmen dieses Knaben gezeigt. In „Das menschliche Auge und seine Erbanlagen" (*Nijhoff*, Haag 1932) zeigt Abb. 18, S. 51, dessen dreieckige Lidspalte, die früher von *Isakowitz* bei 3 Familienmitgliedern als sehr seltenes Merkmal beschrieben worden war. Es ist nicht möglich gewesen dieses Krankheitsbild einer näheren und eingehenderen Betrachtung zu unterwerfen und es weiteren Kreisen bekannt zu machen, da die Eltern des erwähnten Falles eine Röntgenuntersuchung hartnäckig verweigerten und da in allen seitdem vergangenen Jahren kein neuer Fall in unsere Beobachtung kam.

Zweier Ursachen wegen möchten wir auf diesen Fall zurückkommen. Erstens ist es das Verdienst von *Franceschetti* und *Zwahlen* gewesen, daß sie das Krankheitsbild eingehender beschrieben und ihm einen Namen verliehen haben und zweitens ist es uns gerade in letzter Zeit möglich gewesen, 4 neue Fälle dieser merkwürdigen typischen Abweichung untersuchen und mit einander vergleichen zu können.

Der von mir (*Waardenburg*) beobachtete 7jährige Patient, der inzwischen erwachsen ist, kam nämlich zu dem Ohrenarzt Dr. *Navis* mit harmlosen Klagen und wegen seiner Schwerhörigkeit und, als dieser Kollege sich wegen der auffallenden Anomalie mit mir in Verbindung setzte, haben wir die Gelegenheit benutzt, den Fall eingehender zu untersuchen, wobei wir glücklicherweise nicht mehr auf

großen Widerstand des Patienten stießen. Dr. *Navis* glückte es schon innerhalb von zwei Jahren, einen neuen Fall, ein 4jähriges Mädchen, entdecken zu können. Schließlich teilte Dr. *Roesink* an *Waardenburg* mit, daß er wahrscheinlich einen weiteren Fall ermittelt habe. Es handelte sich um eine Frau, die wegen presbyopischer Beschwerden um Rat zu ihm gekommen ist und hierbei berichtet hatte, daß die in Frage kommende Abweichung in ihrer Familie mehrfach vorgekommen sei. Ich konnte die betreffende Familie besuchen, wobei ich noch zwei andere Familienmitglieder fand, welche dieselbe Anomalie aufwiesen.

Franceschetti und *Zwahlen* sind in der Lage gewesen über Fälle mit dieser Anomalie verfügen zu können und haben sich dadurch veranlaßt gesehen alle derartigen Fälle, die sie in der Literatur finden konnten, zu sammeln. Sie haben das Syndrom unter der Bezeichnung *Dysostosis mandibulofacialis* weiter bekannt gemacht. Man kann nicht fordern, daß eine kurze Bezeichnung alle Teilsymptome eines Komplexes enthält, wohl aber, daß er das Wichtigste hervorhebt und die regelmäßigsten Erscheinungen umfaßt. Die genannte Bezeichnung scheint mir ziemlich gut gewählt zu sein, da die Anomalie wesentlich auf dysostotischen Prozessen, hauptsächlich im Unterkiefer und Jochbein beruht, und da mit facialis die übrigen Abweichungen der Lidspalte und des Ohres in ihr angedeutet werden.

Nach *Franceschetti* und *Zwahlen* besteht die Anomalie aus folgenden Einzelsymptomen: 1. Die Lidspalten haben eine antimongoloide Stellung und eine Dreieckform durch Einkerbung oder Andeutung eines Koloboms im äußeren Drittel des Unterlides, so daß ein mehr oder weniger vertikal gerichtetes drittes Augenlid auf der temporalen Seite vorgetäuscht wird. Die Wimpern des Oberlids sind häufig verstärkt und wachsen unregelmäßig, während sie am Unterlid sehr dürftig vorhanden sind. 2. Der Unterkiefer ist hypoplastisch, so daß das Kinn zurückweicht. Der Oberkiefer kann ebenfalls etwas unterentwickelt sein, steht aber dabei gewöhnlich etwas vor (leichter Prognathismus), während damit häufig Zahnanomalien, offener Biß und Palatumabweichungen verbunden sind. 3. Das Jochbein ist atrophisch, häufig bilateral und in verschiedenem Grade, was eine geringe Asymmetrie verursachen kann und eine laterale Vertiefung des Orbitalrandes bedingt. 4. Das äußere Ohr kann malformiert sein und steht gewöhnlich tief. Häufig liegt eine Atresie des äußeren Gehörganges vor. Das Mittelohr und das innere Ohr sind gewöhnlich intakt. Die Abweichungen sind nicht immer beiderseits vorhanden; sie sind oft ungleich stark ausgeprägt. 5. Der Nasenrücken ist gewöhnlich erhöht

und kräftig entwickelt. Der nasofrontale Winkel ist vergrößert (griechische Nase). 6. Mehr accessorische Anomalien sind: große Sinus frontales, Macrostomia mit Blindfisteln in der Linie zwischen Mundwinkel und äußerer Ohröffnung, tiefer Haaransatz vor den Ohren.

Die kritische Zeit des Entstehens dieser komplizierten Anomalie wird auf die Zeit ungefähr nach der 7. Embryonalwoche verlegt.

Wir möchten hier unsere eigenen Befunde mitteilen.

FALL I. (Abb. 1). Nach *Waardenburg*'s Beschreibung, 1932: Eltern normal, nicht verwandt. Knabe: Lidspalten schief von innen-oben nach außen-unten gerichtet. Unterlid temporal-unten auf beiden Seiten abgeknickt und eingekerbt, so daß er den Anschein erweckt, als ob ein etwa 6 mm langes, nahezu vertikal gerichtetes drittes Augenlid, die beiden anderen von einander trennt. Die oberen Augenlider tragen lange Wimpern, die „Schaltstücke" besitzen 2–4 abstehende Wimperhaare, die unteren Augenlider nur wenige feine Wimperhaare im temporalen Drittel, sonst nur noch einige Lanugohaare. Die oberen Tränenpunkte sind normal vorhanden, die unteren fehlen, was Epiphora verursacht; die Carunculae und Plicae semilunares sind etwas nach medial-vorne verzogen, so daß die inneren Augenwinkel sich ungenügend an die Augen anschmiegen, was wahrscheinlich mit einer starken Entwicklung des Nasenrückens zusammenhängt. Es sind merkwürdige Abweichungen der Ausbildung des Gesichtes vorhanden, das seinerseits im Vergleich zu dem normalen mesocephalen Schädel (Index 80.5) ziemlich klein ist. Die Stirn ist niedrig, die Haargrenze geht bis zu den Ohren herunter, die Jochbogen sind hypoplastisch und durch eine niedrig gelegene Spalte von der orbitalen Begrenzung des Os frontale getrennt, der proximale Teil des Oberkiefers ist eingesunken und der untere Orbitalrand nach temporal-unten ausgebuchtet, so daß der Eindruck entsteht, daß die ganze Partie des Gesichtes unter und außerhalb des Auges eingezogen ist. Das Gebiß ist schlecht entwickelt, der Unterkiefer klein, dagegen die Unterlippe dick umgestülpt; das Kinn ist wenig ausgebildet, die Ohren groß und stark abstehend, tief angeheftet, die Ohrenläppchen sind größtenteils mit der Wangenhaut verwachsen.

Bezüglich der formalen Genese und des Zeitpunktes der Entstehung der Anomalie hat *Waardenburg* 1932 bei seinem Fall darauf hingewiesen, daß die Abweichungen Berührungspunkte mit den Verhältnissen, die man im 2.–4. Embryonalmonat finden kann, aufweisen, wenn man davon abgeht, daß der Schädel in diesem Zeitpunkt gewöhnlich noch brachycephal, die Nasenwurzel dann noch relativ breit, aber eingesunken ist. Diese Anomalie darf man nicht auf eine direkte Fixation fetaler Verhältnisse zurückführen, da die normale embryonale Entwicklung eine derartige Form des Unterlides nicht kennt. *Waardenburg* stellte sich wahrscheinlicher vor, daß eine primäre Dysostosis in den die Augenhöhle lateral und unten begrenzenden Skeletteilen, die Ausbildung und den Anschluß der Unterlider verhindert und auch die normale Ausbildung der Bänder des Ligamentum canthi laterale erschwert hat, wodurch das in seiner normalen Entwicklung gestörte Unterlid zu weit nach außen-unten fixiert und eine kolobomähnliche Störung begünstigt wurde. *Waardenburg* hat daran erinnert, daß *Isakowitz*, der im Gegensatz zu ihm eine Vererbung festgestellt hat, ein atypisches Lidkolobom annahm, aber die Möglichkeit einer exzessiven Ausbuchtung des temporalen Lidteiles, wegen ungenügender Ausbildung des Orbitalrandes, ebenfalls erwogen hat.

Navis konnte, wie erwähnt, diesen Fall im Jahre 1946, im Alter von 23 Jahren, erneut untersuchen und seine Befunde jetzt auch mit Röntgenaufnahmen und mit neuen Photographien belegen. Hierbei haben sich keine wesentlich neuen Gesichtspunkte ergeben; nur daß große Sinus frontales vorhanden waren und daß gewisse Einzelsymptome noch stärker zum Vorschein gekommen sind. Wenn man die beiden Profilaufnahmen in verschiedenem Alter vergleicht, sieht man, daß das äußere Ohr eher noch etwas niedriger steht, der Nasofrontalwinkel ist noch mehr im Sinne der griechischen Nase ausgeglichen und das Kinn weicht noch mehr zurück. Das ganze Profil sieht noch mehr wie das Vogelgesicht der vorderasiatischen Rasse aus. Der Gaumen ist schmal und sehr hoch, der Eingang zum Nasopharynx sehr eng. Die Unterlippe ist immer noch etwas verdickt, der seitliche Abstand zwischen Augenbraue und Haarbegrenzung schmal geblieben. Die Ohrläppchen haben sich etwas mehr entwickelt. Die Ohrmuscheln sind noch stark abstehend und *nicht völlig symmetrisch:* der Helix und das Corpus anthelicis ist rechts besser entwickelt als links, das ganze Relief ist links flacher.

Die äußeren Gehörgänge sind sanduhrenförmig, am Übergang vom ersten zum zweiten Drittel des Abstandes Porus externus-Trommelfell ist eine Verengerung vorhanden. Das Trommelfell sieht verknittert aus, ein Hammerstiel und Lichtreflex kann nicht unterschieden werden. Der Eingang zum Pharynx und Nasopharynx ist sehr eng. Es besteht eine deutliche Schalleitungstaubheit, hauptsächlich, aber nicht ausschließlich, auf der Baß-Seite (Flüstersprache ad concham, 2 Meter Konversationssprache). Rinne ist beiderseits negativ, so daß es keine Lateralisation gibt. Schwabach beiderseits verlängert. Die untere Grenze des Gehörs befindet sich zwischen 256 und 512, die obere Grenze ist normal. Die vestibulären Reaktionen sind normal.

FALL II. Familienanamnese: der Vater hat in erster und zweiter Ehe einen normalen Sohn, jetzt 14, bzw. 10 Jahre alt, und eine Tochter, jetzt 5 Jahre alt, welche die Anomalie aufweist (Abb. 2–4). Auch dieser Fall ist typisch. Der Nasenrücken ist schon jetzt hoch ausgebildet. Die Lidspalten haben eine leicht antimongoloide Richtung; die linke eine ausgesprochene Dreiecksform; am rechten Auge ist

Abb. 2.

Abb. 3.

Abb. 4.

das „Zwischenstück" kaum angedeutet. Die oberen Wimpern sind kräftig, die unteren dürftig entwickelt. Während die Augenlider rechts besser entwickelt sind, ist die Ohrmuschel rechts verglichen mit der anderen Seite zurückgeblieben. Beide Ohren stehen niedrig, das rechte Ohr hat eine schmälere und etwas längere Incisura intertragica, das rechte Ohrläppchen ist kleiner und mehr verwachsen; Helix, Anthelix, Crura anthelicis, Concha, und Crus helicis sind rechts hypoplastischer als links. Rechts ist fast keine Scapha vorhanden. Das Gehör ist leicht gestört (2 Meter Konversationssprache). Die äußeren Gehörgänge sind stark verengt, so daß das Trommelfell praktisch unsichtbar ist.

Die Jochbogen sind eingesunken. Der Gaumen ist hoch und breit. Die Zähne stehen ziemlich regelmäßig in einer geschlossenen Reihe, aber beim Schließen des Mundes bleibt ein offener Biß (Mordex apertus), durch welchen die Zunge leicht passiert. Prognathismus und Proodontie fehlen. Die oberen Incisivi sind auffallend kurz. Alle Canini sind groß. Die Refraktion beträgt O.D.S.+4 Diptr. Fundus O.D.S. normal. Leichte Exophorie (Schein-Strabismus durch großen Winkel γ).

Die Haare sind normal eingewachsen und die Begrenzung ist normal.

Die Zahnärzte nehmen beim offenen Biß keine einheitliche Aetiologie an. Die Ursache kann sowohl in den Intermaxillaria als in der Mandibula liegen. In unserem Fall ist es etwas unwahrscheinlich, daß die Intermaxillaria, die aus dem Gebiete der medialen, zwischen den hier stark ausgebildeten lateralen Nasenfortsätzen hervorgehen und zum paraxialen Mesodern gehören, gänzlich unterentwickelt geblieben sind. Höchstwahrscheinlich ist hier der Mordex apertus ausschließlich durch rudimentäre obere Incisivi und Hypoplasie des Unterkiefers (und Oberkiefers?) bedingt. Eine hypoplastische Mandibula kann wahrscheinlich durch Masseterwirkung noch mehr gestreckt werden, so daß der Winkel, der normaliter etwa 120 Grad beträgt, sich vergrößert, wobei der vordere Teil des Unterkiefers noch mehr sinkt.

FALL III. Bei diesem Fall, den ich Dr. *Roesink* verdanke, der meiner Beschreibung und Demonstration der anderen Fälle beigewohnt hatte, handelte es sich um eine 46jährige Frau. Status praesens: Orthophorie. Kein Astigmatismus. O. D. und O. S. Hyperm. 1 Dioptr. S. nach Korr. O. D. 6/6 f. O. S. 6/8 r. Die Anomalie ist eine völlig typische (Abb. 5).

Sie ist an der Lidspalte vollkommen symmetrisch ausgebildet. Die Haare sind normal eingewachsen. Der Nasenrücken ist hoch, das Kinn weicht zurück, die

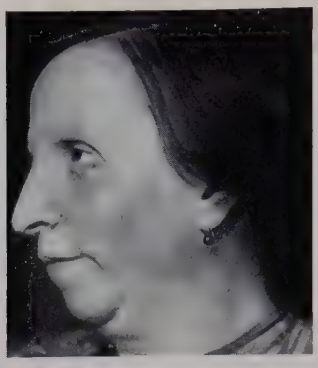


Abb. 5.

Ohrmuscheln sind normal, schmal und sitzen etwas niedrig. Das Gehör ist seit der Kindheit geschwächt, eine nähere Prüfung wurde abgelehnt. Die Jochbogen sind hypoplastisch. Die Verbindung mit den Stirnbeinen ist offen. Der Mund ist etwas verbreitert. Die Zähne sind unregelmäßig und kariös. Das einzige Kind der Patientin starb 1½ Stunde nach der Geburt.

Die Eltern der Frau sowie ihre drei Brüder sind normal. Eine Schwester hatte einen leichten gleichsinnigen Schiefstand der Lidspalten, sonst keine Asymmetrie; ihre drei Kinder sind normal.

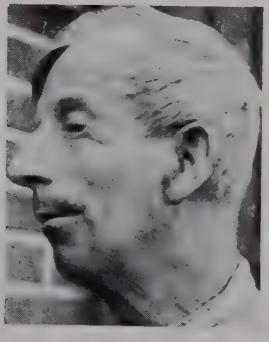


Abb. 6.

Ein Bruder der Mutter der Patientin, z. Z. 69 Jahre alt, zeigt dieselbe Anomalie am Unterkiefer, Kinn und Lidspalte (Abb. 6). Nur ist die Dreieckform rechts sehr schwach angedeutet und besteht mehr in einer leichten Tarsusverdickung als in einer Einkerbung. Die Gehörschärfe ist unter-normal: Rechts Flüstersprache auf 1½, links auf 1 Meter. Schwabach links etwas verlängert, was gegen Labyrinthstörung spricht. Die Untergrenze des Gehörs liegt bei 40, so daß die Möglich-

keit einer Abweichung der Paukenhöhle besteht. Das Trommelfell und der äußere Gehörgang sind normal. Die Ohrmuscheln setzen kaum niedriger als normal an. Der Mund ist ziemlich breit. Der Gaumen ist normal gewölbt. Der Nasenrücken ist hoch. Das Gesicht ist schmal, die Jochbogen schwach entwickelt und am lateralen Augenhöhlenrand fühlt man beiderseits klaffende Spalten über dem Jochbogenansatz. Das Kinn weicht weniger stark zurück als bei der Nichte. Das Gebiß wurde die letzten 4 Jahre schwach. Refr. O. D. Asm 1 vert, O. S. Emm. Patientin ist zweimal verheiratet gewesen. Aus erster Ehe stammen zwei normale Söhne, die zweite Ehe ergab 3 Söhne und 3 Töchter.

Abb. 7.

Abb. 8.

Nur der dritte Sohn, 13 Jahre alt, zeigt die Abweichung in ausgesprochener Form an Kinn, Augenlidern, Jochbeinen und Unterkiefern (Abb. 7, 8). Die äußere Ohrform ist normal, die Einpflanzung etwas niedrig und vor dem rechten Tragus sieht man *einen Auricularanhang*. Die Zähne sind ziemlich regelmäßig. Es besteht ein offener Biß. Der Gaumen ist breit und hoch. Der Nasenrücken ist hoch (leichte Adlernase). Taubheit fehlt. Normale Refraktion. Die Haare beim Vater und Sohn zeigen nichts besonderes.

Die Form der Ohrmuschel bietet bei den drei von der Anomalie befallenen Personen keine Besonderheiten, nur daß die Incisura intertragica bei allen schmal ist und daß der Helix bei der 46jährigen Frau schwach entwickelt ist. Nur beim Knaben stehen die Ohren ein wenig ab.

Während sich in den beiden ersten Fällen keine Vererbung nachweisen ließ, wodurch die Möglichkeit nicht auszuschließen ist, daß die Anomalien durch Mutation neu entstanden sind, war im letzteren Fall ein unregelmäßig-dominanter Erbgang mit geringer Manifestationsschwankung vorhanden. Die drei Träger der Anomalie in dieser Familie III zeigen alle ein scheinbares Außenschielen durch einen positiven Winkel γ wie bei Fall II.

Wenn wir unsere Untersuchungsergebnisse bei diesen 5 Fällen zusammenfassen, so ergibt sich, daß die *Manifestationsschwankungen*

dieses Syndroms *sowohl inter- als intrafamiliär* auftreten, im letzteren Fall hauptsächlich durch *Störung der bilateralen Symmetrie*. Obwohl die Hypoplasien bzw. Anomalien des äußeren Ohres, sowie ihre Ansatz- und Stellungsabweichungen in unseren Fällen wenig ausgesprochen waren (stark abstehende Ohren in Fall I, leicht rudimentäre Ohrmuschel rechts bei Fall II, Auricularanhänge in Fam. III) sind Formen von *Schwerhörigkeit auf Grund von Schalleitungsstörungen*, die im allgemeinen selten sind, festgestellt worden. Die typische Stand- und Formanomalie der Augenlider war in 3 Fällen vollkommen symmetrisch, in 2 Fällen asymmetrisch vorhanden, dagegen klafften die Nähte zwischen Jochbein und Vorderhauptsbein in allen Fällen beiderseitig und die Jochbeine waren stets beiderseitig hypoplastisch ausgebildet. Die Hypoplasie des Unterkiefers und des Kinnes waren wohl stets vorhanden, aber diese Teile waren verschiedengradig rückgebildet. Hypoplasie des Oberkiefers bestand nur bei Fall I.

In dieser Hinsicht *verhält sich* die Dysostosis mandibulofacialis *wie viele in der frühen Embryonalzeit entstehenden Hemmungsmißbildungen*, wie die Augenkolobome, die Nasenscharte und andere Spaltbildungen, die Dysrhaphien inklusive Spina bifida, Mißbildungen des Herzens, des Darmes und des Urogenitalapparates. Unsere klinischen Krankheitsbilder sind im allgemeinen nicht durch Familienforschung, sondern durch statistische Auswertung eines heterogenen Gesamtmaterials entstanden und zwar häufig auf Grund einer zufälligen Duplizität der Fälle oder von zeitlich mehr oder weniger weit entfernten Einzelbeobachtungen. Die nachträgliche Erbforschung hat dann *vielfach nachgewiesen, daß unser klinisches Bild nur die extremen Maximum-Varianten umfaßt*, während die Minus- und Minimumvarianten unserer klinischen Beobachtung entgangen sind. Das hat z. B. für Keratoconus, Hüftluxation, Otosklerose, Epilepsie u. a. wie auch für manche Spaltbildungsanomalien gegolten und scheint ebenfalls für die Dysostosis mandibulofacialis in gewissen Maßen zuzutreffen. *Auch hier gibt es* isolierte (sporadische) und intrafamiliäre *Grenzfälle* (formes frustes, minor variations). Wir glauben, daß wir auf Grund unserer Kenntnisse der embryonalen Ontogenese und unserer erweiterten Analyse der die normale Entwicklung steuernden Erbfaktoren auch gar nichts anderes erwarten können.

Wenn es Gene gibt, die bei der normalen embryonalen Entwicklung gleich- oder ungleichzeitig an verschiedenen örtlich entfernten Stellen eingreifen, so kann die betreffende Genstörung sich nur dann an allen diesen Stellen gleichartig auswirken, wenn die dort erreichten

Entwicklungsphasen genau dieselben sind. Wenn sie das aber entweder durch äußere epigenetisch wirkende Einflüsse mechanischer, chemischer oder blutversorgender Art oder durch das Hineinspielen von individuell-verschiedenen vererbten Nebengenen nicht sind, so wird das betreffende Gen manifestationslabil werden. Wir kennen Erbabweichungen, bei welchen das krankmachende Gen (oder die Abwesenheit bzw. Translokation des normalen Gens) sich unter allen Umständen ähnlich äußert, da es, wie z. B. beim Albinismus, die Vorbedingung für alle weitere Entwicklung enthält. Fehlt die enzymatische Grundlage der Pigmentbildung überhaupt, so kann auch die größte Anzahl von weiteren Pigmentationsfaktoren nichts mehr ausrichten, was mit sich bringt, daß der Albinismus bei allen verschieden pigmentierten Rassen gleichartig monogen bedingt auftritt. Bei der Dysostosis mandibulofacialis scheint dies nicht der Fall zu sein.

Befassen wir uns einen Augenblick mit der *Entwicklung des äusseren Ohres*. Im Jahre 1926 hat *Dahlberg* festgestellt, daß beide Ohren derselben Person durchschnittlich mehr von einander abweichen als ipsolaterale Ohren eines E. Z. Man muß deshalb modifizierende Einflüsse annehmen, und es hat sich ergeben, daß diese sich bei der Ausbildung von Cymba und Cavum conchae, Crus Helicies, Anthelix und Crura Anthelicis, sowie für das übrigens erbliche Darwinsche Höckerchen, das sogar einseitig vorkommen kann, geltend machen können. Zu den modifizierenden Einflüssen gehören die Körperseite, die Gewebserschlaffung des hohen Alters und das Geschlecht, wobei man nicht weiß ob das letztere direkt als Nebengen oder hormonal wirkt. Es gibt z. B. Geschlechtseinflüsse beim Verwachsensein des Ohrläppchens, bei der Ohrenbreite, beim Abstehen der Ohren, ein in Europäer-Kisaresenkreuzung offenbar dominantes Merkmal (*Rodenwaldt*), das überhaupt bei Mädchen viel häufiger und deutlicher zutage tritt. Dies bedingt, daß die Diskordanz von Pärchen (P. Z.) gegenüber derjenigen von gleichgeschlechtlichen Z. Z. wesentlich erhöht ist.

Gerade die Zwillingsforschung hat aber nachgewiesen, daß es demgegenüber eine beträchtliche Anzahl genbedingter Merkmale der äußeren Ohrform (nach *Quelprud* 10–15 Gene) gibt, da in vieler Hinsicht die Diskordanz der E. Z. merkwürdig viel geringer war als die der Z. Z. (*Volta* 1924, *Geyer* 1926–1936, *Quelprud* 1932–1935). Deshalb wird die Ohrform bei der Vaterschaftsbestimmung mitberücksichtigt. Belangreiche Erbmerkmale des Ohres sind 1. die Stellung und Einpflanzung, 2. die Ohrlänge, 3. der Entwicklungsgrad, Ausdehnung, Anfang und Form des Helix, 4. die Ausdehnung der Scapha zwischen

Helix und Anthelix nach unten bis im Ohrläppchen, 5. die Form und Biegung des von einander unabhängigen Tragus und Antitragus und die Länge und Breite der Incisura intertragica sowie ihre Richtung gegenüber der Frankfurter Horizontalen, 6. der Insertionswinkel d. h. der Winkel zwischen der Längsrichtung des Ohres und der Frankfurter Horizontale, 7. die Länge, Größe, Dicke und Form, sowie der Ansatz und die Verwachsungsart des am spätesten zur Entwicklung kommenden Ohrläppchens, 8. die Ohrenbreite. Auch leichte Anomalien können erblich sein, wie z. B. eine Knorpelverdickung beim Ansatz der Ohrmuschel hinter der Cymba conchae und eine Leiste (crus) in der Cymba (Mozartohr), sowie kleine Fisteln, eine Incisura anterior über dem Tragus, das Tuberculum Darwini, und ein extra Tuberculum supratragicum, für welches letztere E. Z. stets konkordant sind.

Es ist klar, daß auf dieser Erbgrundlage eine Menge individueller, polygen bedingter Ohrformen entstehen kann, was zusammen mit den Modifikationen veranlaßte, daß die Ohrenform schon vor 1906 *zu Identifikationszwecken propagiert* wurde. Es ist *ebenfalls einleuchtend, daß diese individuellen Erbmerkmale sich nur dann äußern, wenn eine ebenfalls ererbte Grundbedingung der Ohrenentwicklung überhaupt erfüllt ist.* Je früher die Anlage des äußeren Ohres in ihrer Entwicklung gestört wird, desto unschärfer läßt sich am rudimentären Ohr der Enderfolg definieren und um so unsicherer vorhersagen. Es hat sich ergeben, daß die Microtie an sich vererbbar ist, daß aber dabei ein sehr buntes phänotypisches Bild auftreten kann, wie dies *Gaus* bei einer Familie beschreiben konnte; hierbei bleibt es unentschieden, inwieweit rein äußere Einflüsse oder die genetische Restkonstitution diese Vielfältigkeit verursacht hat. In einer anderen Familie fand *Gaus* eine Begrenzung der Ohrmuschelanomalie auf das männliche Geschlecht und zwar auf alle Männer in 4 Generationen, so daß der Eindruck entstand, sie sei am Y-Chromosom gebunden. Auf Grund fehlenden Interesses liegen leider bisher keine zahlreichen Untersuchungen über erbliche Abweichungen des äußeren Ohres vor. Es wurde Microtie bei Bruder und Schwester (*Burger*), malformierte Ohrmuscheln bei 8 von 23 Familienmitgliedern (*Czörsz*), Microtie mit Atresie des Gehörganges bei Vater und Sohn (*Frenzel*), ein- und doppelseitige Malformation des Ohres mit Atresie bei mehreren Familienmitgliedern (*Schwarz*) beschrieben. Die Atresien können zuweilen ebenfalls ohne Ohrmuschelabweichungen familiär-gehäuft vorkommen (*Krampitz, Eckert, Möbius, von Bracht, Torrigiani, Potter*

(5 Geschlechter). Als weitere Erbabweichungen können ein korkzieherartiger Meatus (*Stetter*), Ohrenfisteln (*Eyle* u. a.), Hypertrichosis der Innen- und Außenseite des Ohrmuschels, und zwar nur bei Männern (*Tommasi*), sowie Auricularanhänge, einmal mit Polyotie verbunden (*Bol* und *De Kleyn*) vorkommen.

Es ist *deshalb nicht erstaunlich, daß die Dysostosis mandibulofacialis bei verschiedenen Personen eine ausgesprochene Variabilität der Störungen des äußeren Ohres zeigt*, wenn wir sehen, wie ungesetzmäßig diese schon in ein und derselben Familie auftreten kann. Die besten Belege dafür ergibt das von *Franceschetti* und *Zwahlen* aus der Literatur gesammelte Material. Wie in ihrem eigenen typischen Fall sehen wir die Manifestationsschwankungen entweder bilateral als Modifikationen oder interfamiliär, wahrscheinlich erblich mitbedingt, auftreten. Die Häufigkeit der einseitigen oder asymmetrischen Ohrenabweichungen (*Pires de Lima*, *Monteiro*, *McEnery* und *Brenneman*, *Franceschetti* und *Zwahlen* u. a.) beweist u. E., daß bei dieser eingreifenden frühzeitigen Hemmungsmißbildung exogene Umstände stark mitbestimmen, ob und in welchem Ausmaß Erbfaktoren noch einen Einfluß auf die Ohrenform ausüben können.

Um sich die weiteren Vorgänge besser klar zu machen, kann man noch *die normale embryonale Entwicklung* heranziehen. Man soll sich dabei vergegenwärtigen, daß auch diese nicht schablonenhaft verläuft, daß sie aber auf Grund individuell verschiedenartiger Genome (Gesamterbanlagen) Unterschiede aufweist. Man muß annehmen, daß *die während des 4. Monats mehrmals festgestellten individuellen Verschiedenheiten* (*Retzius*) schon viel früher anfangen, als sie vom Forscher festgestellt werden können und daß die Nebengene bewirken, daß die Determinationspunkte der Spezialisierung der Gewebe und Organe nicht bei allen Individuen und nicht für alle Merkmale genau in dieselbe Zeitfrist fallen. Dies bedingt, daß die polyphän zur Auswirkung kommenden pathologischen Gene *bei einem Individuum alle* betreffenden Zellgruppen zu gleicher Zeit beeinflussen, *bei anderen nur einen Teil* derselben. So kann bei der Dysostosis mandibulofacialis das eine Mal eine bestimmte Teilerscheinung, das andere Mal eine andere überwiegend oder allein zum Vorschein kommen, während ein drittes Mal das ganze Syndrom zutage tritt.

Das Krankheitsbild, das uns jetzt beschäftigt, ist *dadurch eigentümlich, daß seine Teilerscheinungen wahrscheinlich alle in einer bestimmten embryonalen Periode entstanden sind.*

Es ist bekannt, daß die embryologische Entwicklung der Augenlider und des äußeren Ohres zeitlich nicht weit auseinander liegt. Häufig beginnen sie sich in dem 2. Embryonalmonat bei einer Sch.-St.-Länge von ca. 17 mm gegen Ende der 6. Woche zur selben Zeit auszubilden; öfters auch fängt die Bildung der Lider gleich nach derjenigen der Ohren an. So ist es nicht zu verwundern, daß erbliche Hemmungsmißbildungen der Lider und der Ohren auch gesondert vorkommen können.

Gegen Ende des 2. Monats, bei einer Sch.-St.-Länge von 20–23 mm sind Helix und Anthelix, Tragus und Antitragus zu unterscheiden, aber erst im Anfang des 3. Monats (25–50 mm) ist eine teils freie, teils noch verwachsene Ohrmuschel vorhanden, ohne Ohrläppchen, das nach *Schaffer* gegen den 4. Monat noch in 80 Prozent der Fälle fehlt. Das äußere Ohr bildet sich am Boden und in der Umgebung der 1. Kiemenfurche, also aus dem Mandibular- oder 1. Kiemenbogen und aus dem Hyoid- oder 2. Kiemenbogen. Im Laufe des 2. Monats (10–17 mm in der 4., 5–6. Woche) entsteht die Fossa conchae als eine Vertiefung der Mitte der Kiemenfurche, wobei sich drei Teile übereinander ausbilden: die Fossa intertragica unten, die Cymba conchae oben und dazwischen das Cavum conchae, die zusammen den mit der Schläfe verwachsenen Teil der Ohrmuschel bilden. Bei Embryonen von circa 16–17 mm wächst der primitive Gehörgang als eine trichterförmige Hohlröhre aus dem Cavum nach innen in die Richtung des Innenohres, das aus dem schon sehr früh hinter dem dorsalen Teil des 1. Kiemenbogens entstandenen Gehörbläschens hervorging. Zu Beginn der Entwicklung des äußeren Ohres sind die weiteren Differenzierungsvorgänge des häutigen Labyrinthes in Bogengänge und Ductus cochlearis schon abgeschlossen. Es ist deshalb nicht sehr wahrscheinlich, daß eventuelle Gehörstörungen bei der Dysostosis m. f. auf Innenohrschwerhörigkeit beruhen. Man wird eher Störung der schallleitenden Organe erwarten.

Ungefähr gleichzeitig mit der Ausbildung des Gehörganges entsteht bei Embryonen von 10–20 mm vor der Fossa conchae sowohl im Mandibularbogen als im Hyoidbogen eine Reihe von 3 Auricularhöckerchen. Tragus und Antitragus entstehen aus den einander gegenüber liegenden unteren Höckerchen, während die beiden vorderen oberen Höckerchen das Crus helicis mit dem Helix ascendens und die beiden hinteren oberen Höckerchen den Anthelix bilden. In der 5. Woche entsteht hinter den hinteren Ohrhöckerchen im Hyoidbogen eine Falte, als Anlage des freien Ohrrandes, aus welcher ungefähr

gleichzeitig mit der Bildung des Anthelix der Helix descendens hervorgeht (Sch.-St.-Länge 14–16 mm). Bei einer Länge von plm. 20 mm ist deshalb der freie Teil der Ohrmuschel als sogenanntes Ober- und Unterohr zustande gekommen.

Gelegentlich werden Kinder geboren, die vor der Ohrmuschel Fibrochondrome, als sog. *Aurikularanhänge* besitzen. Es sind in der Tierreihe, z. B. bei Ziegen, Schafen und Schweinen, bekannte Gebilde: Glocken oder Aurikeln genannt. Beim Menschen werden sie einer Dislokation der Aurikularhöcker zugeschrieben. Bei den genannten Tieren sind es dominante, gelegentlich einseitige Merkmale. Diese gewöhnlich einigermaßen gestielten Auswüchse besitzen einen harten Knorpelkern. Ihre Entstehung beim Menschen deutet auf eine frühe Entwicklungsstörung, vielleicht schon in der 5.–6. Woche, hin und könnte nur dann später angenommen werden, wenn es sich ergeben würde, daß sie auch auf nachträgliche Abspaltung von Knorpelteilen beruhen kann. Ohrfisteln können branchiogen entstehen, wenn die erste Kiemenfurche sich abnorm wenig schließt. Eine Atresie des äußeren Gehörganges wird auf örtlich vollständigen Verschluß dieser Kiemenfurche zurückgeführt. Wir glauben, daß sowohl der von uns in einem Fall einseitig angetroffene Aurikularanhang als auch die mehrmals beobachtete rudimentäre Ausbildung, Verengerung oder Atresie des äußeren Gehörganges in Fällen von Dysostosis mandibulofacialis (*van Lint* und *Henneberg*, *Mc Enery* und *Brennemann*, Pomfret *Kilner*, *Franceschetti* und *Zwahlen*) auf eine frühe Entwicklungshemmung deuten. Dasselbe gilt für alle Fälle, wo Microtie oder starke Malformation und Tiefstand der Ohrmuschel vorlag, wie *Waardenburg* es ebenfalls bei einem ihm liebenswürdigerweise von Prof. *Hanhart* gezeigten schweizerischen Mädchen beobachten konnte. Die Tatsache aber, daß auch eine stärkere derartige Anomalie gleich wie die Paukenhöhlenverbildung, oder das abstehende und das Darwinsche Ohr einseitig oder rechts und links verschiedengradig ausgeprägt, d. h. *eine deutliche bilaterale Asymmetrie aufweisen* kann, *beweist, daß die Entwicklung des äußeren Ohres beidseitig nicht immer im selben Tempo stattfindet* oder daß das normale Allel bei Heterozygoten bilateral verschieden zur Geltung kommt. Das erschwert die genaue Bestimmung des Zeitpunktes der Ohranomalie und gibt einen Spielraum von der 5.–7. Embryonalwoche. Die Schalleitungstaubheit in einer Anzahl von Fällen ist durch diese Befunde genügend erklärt. Etwas schwieriger ist die Deutung des von *Ida Mann* für ihren Fall angenommenen Fehlens der Paukenhöhlen und der Mastoidzellen und besonders die Deutung

der Anomalie der Cochlea ("the cochlea seems on both sides not to be formed properly", "the bony labyrinth is normal"). Die Cochlea entsteht nämlich schon bei Embryonen von cirka 12 mm. Sch.-St.-Länge (35 Tage). Die Fehlbildung des Mittelohres ist wohl häufig mit äußeren Ohranomalien verbunden, da die Trennung von Rachen und Mittelohr bei Embryonen von 18–24 mm (6–6½ Wochen) zustande kommt und also in dieselbe Zeitfrist fällt. Es ist dann aber unerklärlich, daß in *Mann*'s Fall das äußere Ohr intakt ist.

Wenn man die Malformation der Ohrmuschel und die Mikrotie auf einen Hemmungsfaktor zurückführt, *wie läßt sich dann die gelegentlich gefundene Macrotie* (*Collins*, *Mann*, *Isakowitz*, *Johnstone*, *Waardenburg*, u. a.) *und das Abstehen der Ohren erklären?* Man kommt hier u. E. am weitesten, wenn man bedenkt, daß *jede embryonale Entwicklung*, besonders in den ersten Monaten, *mit einer fortwährenden Wachstumsbeschleunigung in einem und einer Hemmung im nächstliegenden Gebiete einhergeht.* Das trifft für benachbarte Gebiete zu, wie z. B. Augengegend und Nasenwurzel (*Waardenburg*), aber ebenfalls für Unterteile desselben Organs, wofür die normale Nasenentwicklung das beste Beispiel liefert. So wäre es deswegen denkbar, daß am äusseren Ohr in einem gewissen Stadium der anormalen Entwicklung, neben einer vielleicht beschränkten örtlichen Retardation eine Propulsion oder Hyperplasie bemerkbar wird. Je relativ später die Hemmung im Kiemenbogengebiet auftritt, je wahrscheinlicher ist die Chance für eine derartige reaktive Hyperplasie der Ohrmuschel. Andere Beispiele für eine solche Hyperplasie bei der D. m. f. sind möglicherweise: der Haarzipfel vor den Ohren, die verstärkte Wimperbildung des Oberlides (wobei eine gelegentlich vorhandene leichte Einziehung des Oberlides vielleicht damit zusammenhängt, daß eine Zeit lang keine Berührung mit der korrespondierenden Stelle des Unterlides bestand), Auricularanhänge, vielleicht als Ausdruck einer rudimentären Polyotie, hyperplastische Nasenwurzel mit großem Sinus frontalis.

Läßt sich die Entstehungszeit der Ohranomalien mit derjenigen der begleitenden Anomalien des Unterkiefers, des Jochbeins und der Augengegend vereinbaren?

Die Hypoplasie des Unterkiefers ist bei einer derzeitigen Entwicklungshemmung im 1. und 2. Kiemenbogengebiet sicher zu erwarten. Da der Unterkiefer erst im 3. Monat seine definitive Form erreicht, wird eine frühere Störung mit einer Unterentwicklung der

Mandibula einhergehen. Tritt sie sehr früh auf, z. B. im Stadium des Meckelschen Knorpels, so kann auch der damit verbundene Hammer leiden. Schon in der 2. Woche ist der Mandibularbogen als untere Begrenzung der Mundbucht gebildet. In der 3. Woche entsteht aus ihm heraus ein Oberkieferfortsatz. In der Mitte des 2. Monats wird die Kinnanlage als ein rundlicher Höcker schwach markiert. Beim Rind sind Auricularanhänge aufgetreten in Zusammenhang mit einem recessiv-erblichen Fehlen des Unterkiefers (*Ely*, *Hull* und *Morrison*), und *Stupka* hat eine komplette Fehlbildung beim Menschen abgebildet, wo tiefstehende Ohren mit Agenesie des Unterkiefers, bilateralen Wangenspalten, Cheilo- (rechts) und Cheilognathopalatoschisis (links) usw. verbunden sind. Dies erinnert an die von *Franceschetti* und *Zwahlen* erwähnten *Wright*'schen Inzuchtversuche bei Meerschweinchen, wo leichte bis schwergradige Otocephalie (Dysplasie des Angesichts mit Fehlen des Unterkiefers) vorkam, einmal sogar ein Monstrum *ohne Jochbogen*, *Mandibula*, *äußeren und inneren Ohren* und mit *sehr kleinem Oberkiefer*, sowie an die von *Wolff* durchgeführte Radiumbestrahlung des Mesencephalon von Hühnerembryonen, wo entweder *Micrognathie*, oder Otocephalie mit *Fehlbildung des äußeren Gehörganges*, oder auch *Macrostomie* entstand, die zuweilen mit *Atrophie der unteren Augenlider* und sogar u. U. mit leichtem Microphthalmus verbunden war.

Wir möchten hier auch noch eine Beobachtung erwähnen, die einer von uns bei einem 1947 in Arnhem geborenen *Doppelmonstrum* männlichen Geschlechts mit Hydramnion machen konnte. Es handelte sich um abnorm große Fissurae abdominales, Bauchspalten oder Bauchbrüche mit Eventration beider Zwillinge, wobei die Baucheingeweide im Exocölom in direkter Berührung mit dem Chorion der Placenta lagen, so daß der gewöhnliche dünne Nabelstrang fehlte. Beim rechten Zwilling war der Bruch auf den Bauch beschränkt, beim linken Zwilling hatte er sich mit einer Fissura thoracis kompliziert. Dazu kam noch eine Verwachsung der rechten Bauch- und Brustseite des linken Zwillings mit den linken gleichen Teilen des rechten Zwillings, wo die mittlere Rückengegend auch streckenweise hineinbezogen war (asymmetrischer, teilweiser Ileothoracopagus). Der rechte Zwilling hatte eine starke Zwangsdrehung dem linken gegenüber. Es machte den Eindruck als ob der linke Zwilling sich mit seinem Kopfe in das Peritoneum oder Mesenterium des rechten hineinverfangen hätte, jedenfalls war dieses wie eine straffe enge Haube über seinen Kopf gespannt.

Der rechte Zwilling hatte einen normalen Kopf. Als äußere Anomalien waren bei ihm ein linksseitiger Pes varus und eine doppelseitige leichte Blepharophimosis mit Dystopia canthi medialis lateroversa vorhanden. Der linke Zwilling hatte starke Fehlbildungen: ein kurzes rechtes Ärmchen mit Ectrodactylie, die linke Hand hat 4 Finger und einen schlaff hängenden kurzen Daumen, es besteht doppelseitiger Pes varus. Das Gesicht ist grob deformiert im Sinne einer Otocephalie. Rechts Anophthalmus und eine kurze Querfurche als Andeutung einer Lidspalte. Nase formlos verdickt, das rechte Nasenloch und ein Septum nasi fehlt. Links Cheilognathoschisis und offene Gesichtsspalte, so daß man den linken Flügel der rüsselartigen Nase abheben kann und in den weiten Nasenraum schaut. Links am Auge: Zentrale Hornhauttrübung; *fehlende Augenlider, Karunkel und Plica semilunaris*, gequollene Conjunctiva bulbi, weiter: metopische Naht, temporaler Defekt des 1. Os frontale. Beiderseits *fehlen die Ohrmuscheln*, unten besteht eine breite klaffende Spalte zwischen beiden Mandibularbogen, so daß man in den Rachen hineinschaut, *beide Unterkieferhälften* sind *hypoplastisch, die linke ist rudimentär.*

Im Jahre 1934 hat *Waardenburg* ein Kind mit Acrocephalosyndaktylie und einer Menge anderer angeborener Hemmungsmißbildungen beschrieben, darunter auch *Hypoplasie der Unterkiefer und des Kinns, malformierte tiefstehende Ohren*, relativer Prognathismus des Oberkiefers, große Nase und antimongoloider Schiefstand der Lidspalten.

Bolloli (s. *Strupler*) beschreibt eine E. Z. Geburt, wobei das eine Kind gut ausgebildet war, und das andere Kind Hydrocephalus und Gesichtsasymmetrie mit *zusammengerollten nach hinten verlagerten Ohrmuscheln und atrophischen Gehörgängen* zeigte. Die linke Gesichtshälfte zeigt grobe Störungen: wahrscheinlich Anophthalmus, nicht auseinanderspreizbare Augenlider, rüsselartige Nase mit nach rechts abweichender Spitze, *Hasenscharte-Gaumenspalte.*

Zusammenfassend sieht man, daß Dysplasien des Unterkiefers oder der Ohren oder beider, häufig zusammen mit anderen geringeren oder groben Störungen des Gesichtes durch sehr verschiedene Ursachen biochemischer (Vererbung), physikalischer (Bestrahlung) und mechanischer Art (Raumbeschränkung, Zirkulationsstörung) in einer offenbar kritischen frühen Entwicklungsperiode entstehen und sich ebenfalls mit Dysplasie des Jochbeins verbinden können.

Wir möchten jetzt prüfen, ob die Jochbeinstörung in denselben Zeitraum fällt, den wir für die Dysplasie der Ohren und des Unter-

kiefers gefunden haben (17–20 mm). Das kann nur der Fall sein, wenn die bindegewebige Anlage des Jochbeins schon eine dürftige ist. Denn das Jochbein wird zum Belegknochen, und zwar ohne knorpeliges Vorstadium, im Anfang des 3. Monats (Sch.-St.-Länge 31 mm), wobei gleichzeitig die Verbeinung der Ossa frontalia vor sich geht und das Auftreten eines Beinkerns im Schläfenbein in der Nähe des Proc. zygomaticus, der ebenfalls früh verbeint, stattfindet. Das Jochbein nähert sich bald den Proc. zygomatici des Oberkiefers und des Schläfenbeins und geht damit eine bindegewebige Verbindung ein. Erst im Anfang des 4. Monats (Sch.-St.-Länge 80 mm) erreicht das Jochbein das Vorderhauptsbein, womit es sich bindegewebig verbindet. Diese Verbindung kommt bei der Dysostosis m. f. niemals richtig zustande, aber das kann ebenso gut die Folge einer Störung um diese Zeit wie in dem Bindegewebestadium sein. Ober- und Unterkiefer sind die ersten Knochen des menschlichen Schädels, sie verbeinen schon bei 15 mm Sch. St. Länge. Es kann sein, daß die Dysplasie sich auch auf den Oberkieferfortsatz ausdehnt. Die Zahnleisten entstehen bei plm. 25 mm langen Embryonen (7 Wochen), und die Anlagen der Milchzähne treten im 3. Monat auf. Kieferdysplasien in der 5.–7. Woche können also in der 9. Woche von Zahnanomalien gefolgt werden.

Wir kommen schließlich zu der Frage, ob der angenommene Zeitpunkt mit demjenigen der Fehlbildung der Augenlider stimmt. Im Anfang der 7. Woche entstehen bei Embryonen von plm. 17 mm Sch.-St.-Länge bogenförmige Hautfalten, die die vorderen Augenpartien nur peripher umrahmen. Am Ende des 2. Monats ist ein temporaler und am Anfang des 3. Monats ein nasaler Lidwinkel sichtbar, aber erst bei 37 mm Sch.-St.-Länge sind die vorgewachsenen Lidränder von den Winkeln bis zur Mitte verklebt und erst danach entsteht die Marginaldifferenzierung und die weitere Zilien-, Drüsen- und Tarsusentwicklung. Die Zilienanlagen erscheinen erst am Ende des 3. Monats mit denjenigen der Meibomschen Drüsen, die in der 2. Hälfte des 4. Monats noch nicht viel weiter gekommen sind. Das Unterlid wächst mühsamer empor als das Oberlid nach unten. Niemals haben die noch offenen Lidspalten eine Dreieckform wie bei der Dysostosis m. f., aber was regelmäßig vorkommt ist eine Rautenform, wobei die eine Diagonale die Lidwinkel und die andere zwei abgerundete Lidbuchten verbindet, wovon einer medial im Oberlid und einer lateral im Unterlid gelegen ist. Die obere Bucht ist eine Praedilektionsstelle für Lidkolobome und die untere offenbar für die

Einziehung oder Einkerbung der Dyostosis m.f. Die Augenlider haben eine gemischte Herkunft: der Canthus medialis soll aus dem seitlichen Nasenfortsatz hervorgehen, der Rest des Oberlides aus dem Seitenteil des unpaarigen Stirnfortsatzes, der Rest des Unterlides aus dem Oberkieferfortsatz. Das erklärt, daß Kolobome des Unterlides sich zuweilen ebenfalls an derselben medialen Seite befinden, wo man die Dehiszenzen der schiefen Gesichtsspalte antrifft. Kolobome und Gesichtsspaltreste sind selten als erblich verzeichnet (*Pfannmüller*, *Zumsteeg*, *Bishop Harman*).

Wir können uns *von der formalen Genese der Lidanomalie folgende Vorstellung* machen: während der Gehirnschädel von paraxialem Mesoderm umgeben ist, das auch die Sinnesorgane, den oberen Orbitalteil, das Auge, das Oberlid und die Augenwinkel versorgt und bei der Dysostosis m.f. normal vorhanden ist, entstehen das Skelett und die Weichteile des Gesichts hauptsächlich aus dem visceralen Mesoderm, das hier offenbar im Gebiete des 1. Kiemenbogens und im Anschlußgebiet an den Hirnschädel unterentwickelt bleibt. Es gibt nun zwei Möglichkeiten für die abnorme Ausbildung des Unterlides: erstens die vorher von *Waardenburg* vertretene, wobei eine primäre Hypoplasie des Jochbeins die häufig normaliter bis in den 4. Monat vorhandene antimongoloide Lidspaltenrichtung verstärkt und zu gleicher Zeit den temporalen Teil des Unterlides durch ein schief nach unten gerichtetes Ligamentum canthi laterale, das sich an ein Tuberculum auf der Innenseite des Jochbeins anheftet, mechanisch daran behindert emporzuwachsen, so daß eine Einknickung entsteht; und zweitens, daß das viscerale Mesoderm des Unterlides ebenfalls primär unterentwickelt ist und das Vorwachsen am längsten da unterbleibt, wo die Dysplasie des Jochbeins am stärksten ist. Für das Erstere spricht der *Lloyd Johnstone*'sche operative Befund von fibrösen Bändern an der Grenze des mittleren und lateralen Drittels des Unterlides, die man als Reaktion entstanden denken könnte, für das Zweite spricht die weitere Unterentwicklung der nasalen zwei Drittel des Unterlides im Falle *Mann*, wo die marginale und intermarginale Differenzierung, die Wimpern und Meybomschen Drüsen fehlten und das Lid verdünnt war, sowie der erste *Waardenburg*'sche Fall, wo noch die unteren Tränenpunkte fehlten. Es ist nicht unmöglich, daß beide Anomalien zusammen vorkommen können. *Ida Mann* glaubt, daß die Innervation ebenfalls ihre Bedeutung hat: das paraxiale Mesoderm des Antlitzes wird vom ersten Zweig des Trigeminus, das viscerale Mesoderm des Unterkiefers vom dritten Zweig und alles, was da-

zwischen liegt vom zweiten Zweig (mit Ausnahme des äußeren Drittels des Unterlides) versorgt. (Gemäß Erfahrung der Zahnärzte soll bei Injektion des Oberkiefers das Unterlid anaesthetisch werden, und zwar mit Ausnahme der äußeren 2–3 mm). Dies würde eine Erklärung für die geläufige Erfahrung sein, daß das temporale Schaltstück Wimpern trägt und im allgemeinen besser entwickelt ist als der Rest des Unterlides, obwohl man ohne Innervationseinflüsse auch auskommen kann, wenn man annimmt, daß die primäre Hypoplasie des visceralen Mesoderms sich nur auf die nasalen zwei Drittel des Unterlides ausdehnt, und die Einziehung dadurch entsteht, daß dieser Teil das Schaltstück örtlich daran behindert vorwärts zu wachsen. Hier wäre noch zu erwägen, daß zur Zeit niemand weiß, wo die normale laterale Grenze zwischen dem nach *Mann* relativ unabhängigen paraxialen und visceralen Mesoderm liegt. Es wäre nicht undenkbar, daß wenn das Jochbein zum visceralen, das Stirnbein, das Keilbein und die Schuppe des Schläfenbeines zum paraxialen Mesoderm gehören, das äußere Drittel des Unterlides beim letzteren oder beim Grenzgebiet eingereiht werden muß, und so eine eigene Entwicklungstendenz hat.

Wie dem auch sei, *es scheint nichts der Auffassung im Wege zu stehen, daß die dysplastische Störung im Unterlid ebenfalls bei der ersten Lidanlage bei Embryonen von 17–20 mm Sch.-St.-Länge beginnt.* Es ist *nicht unbedingt nötig* – wie gesagt – daß ein polyphänes Gen an den diesbezüglichen embryonalen Bezirken *gleichzeitig* zur Geltung kommt, z. B. wird beim Albinismus sich die Pigmentationsstörung viel eher äußern als das Ausbleiben der Foveaausbildung. So haben *Franceschetti* und *Valerio* eine Augen- (Microphthalmus usw.) und Ohrenmißbildung bei 2 Geschwistern beschrieben, die *ungleichzeitig* angefangen haben. Auch in der Weise wäre es denkbar, daß Erscheinungen eines polyphänen Merkmalkomplexes ausbleiben können, wenn das Gen an diesen Unterteilen abweichende Gesamtkonstellationen antrifft. Auf der Suche nach vergleichbaren Fällen von Lidanomalie wie bei der Dysostosis m. f. sind wir noch auf eine Mitteilung von *Rochat* jr. gestoßen, wo ein Kind eine rechtsseitige offene Gesichtsspalte mit nasalem Kolobom des Oberlides aufwies und links eine Lippenspalte mit nasalen Kolobomen des Ober- und Unterlides und eine temporale Bildung, ähnlich derjenigen der D. m. f. zeigte, was wieder die Erfahrung bestätigt, daß derartige Anomalien in früher Embryonalzeit und gerne gehäuft auftreten.

Auf Grund unserer embryologischen Überlegungen sehen wir uns genötigt die erste Fehlrichtung der Entwicklung des Gesamtbildes

der Dysostosis mandibulofacialis nach der 6.–7. Woche zu verlegen, während Begleit- oder Folgeerscheinungen (fehlerhafte, Jochbeinverbeinung, Differenzierung des Unterlides und seines Randes, Anschluß des Jochbeins an das Vorderhauptsbein), bzw. nach dem Anfang und Ende des 3., sowie dem Anfang des 4. Monats verlegt werden müssen, wie *Waardenburg* das schon in seiner ersten Publikation angegeben hat.

Wir sind nun in die glückliche Lage geraten, daß unsere Anregung die Entdeckung neuer Fälle in den Niederlanden zur Folge gehabt hat. Es handelt sich erstens um den Fall eines 4jährigen Knaben, von dem uns in liebenswürdiger Weise der Augenarzt *Goedbloed* im Haag berichtet hat. Er zeigt die doppelseitige Lid- und Jochbeinanomalie, ein schwach entwickeltes Kinn, keine äußere Ohrenabweichungen oder Taubheit, aber einseitige Atresie des äußeren Gehörganges. (Abb. 9). Weitere Fälle kamen in dieser Familie nicht vor.

Abb. 9.

Der zweite Fall einer 58jährigen Frau wurde uns vom Augenarzt *Pameyer* aus Deventer vermittelt. Die Mißbildung besteht hier in sehr ausgesprochener Form, ebenfalls an beiden Ohrmuscheln, wie die Abb. 10 und 11 uns zeigen. Ob die begleitende Gehörstörung nur auf Schalleitungsstörung oder außerdem auf Labyrinthstörung beruht, konnte man noch nicht mit Sicherheit feststellen. Mittels einer

Abb. 10. *Abb. 11.*

Photographie wurde erwiesen, daß die schon verstorbene Mutter (Abb. 12) wahrscheinlich die Überträgerin der Anomalie war, da sie links ein deutliches Schaltstück, rechts ein leichtes Ektropion mit geknicktem Lidrand darbot. Der Nasenrücken scheint hoch zu sein, der Mund ist breit. Es mag sich hier wohl um einen Grenzfall handeln. Leider bedeckt die Bauernhaube die Ohren, sodaß es unmöglich ist zu sehen, ob ihnen etwas fehlt. Man kann sich leicht vorstellen, daß nur die Grenzfälle bei Frauen eine Ehe ermöglichen, da ausgesprochene Fälle wohl wenig Reize auf das männliche Geschlecht ausüben werden.

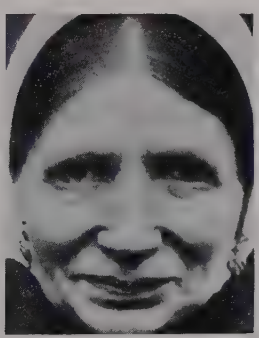


Abb. 12.

Während wir in den beiden ersten von uns beobachteten Fällen sowie im Falle *Goedbloed* nicht wissen wie sie zustande kamen, ist es

sicher, daß in unserem dritten Fall und im Falle *Pameyer eine unregelmäßig bzw. regelmäßig dominant vererbte Mutation* vorlag. Damit reihen sich diese beiden letzten Fälle an andere Literaturbefunde an, z. B. an familiär-erbliche Beobachtungen von *Berry* (Frau bilateral, Tochter unilateral), *Isakowitz* (Vater und 2 Töchter), *Pirés de Lima* und *Hernani Monteiro* (2 Brüder), *Sanvenero-Rosseli* (2 Brüder), *Leopold*, *Mahoney* und *Mabel Lee Price* (Tochter, Mutter, Großvater mütterlicherseits), *Schachter* (Vater und Sohn). Das intrafamiliäre klinische Bild ist variabel. Merkwürdigerweise berichten die amerikanischen Autoren nicht über Hypoplasie der Jochbeine, sondern der Processi zygomatici der Schläfenbeine. In der von *Berry* beschriebenen Familie, die wie diejenige von *Isakowitz* inkomplette Fälle ohne Ohrenabweichungen umfaßt, hatte die befallene Frau in ihrer Jugend noch eine Hasenscharte gehabt. *Franceschetti* und *Zwahlen* haben neben den kompletten auch inkomplette Bilder und neben den typischen auch atypische Formen angenommen. Zu den letztgenannten gehören dann vermutlich auch Grenzfälle ohne die typische Lidanomalie. Auf Grund der beobachteten Einseitigkeit soll man diesen Autoren beistimmen, daß es dann auch doppelseitiges Fehlen geben kann. Eine sichere Beurteilungsgrundlage bekommen wir aber erst durch genaues Familienstudium. Die da eventuell angetroffenen Grenzfälle können natürlich auch isoliert auftreten. Vorläufig scheint uns noch eine reservierte Haltung bei der Differentialdiagnostik geboten. Es ist fraglich, ob jedes Fisch- oder Vogelgesicht hierher gehört.

Eine ähnliche Gesichtsbildung kommt z. B. bei beiden 13jährigen erbgleichen männlichen Zwillingen vor, bei denen *Leonore Liebenam* die Diagnose Dysostosis craniofacialis gestellt hat, obwohl eine kleine Maxilla und Prognathismus des Unterkiefers fehlten, aber gegen D. m. f. spricht, daß die Unterkiefer und Jochbogen nicht hypoplastisch waren und daß die typischen Augenlid- und Ohranomalien fehlten.

Wir wissen, daß mehrere Einzelmerkmale, wie antimongoloide Richtung der Lidspalten, Mikrognathie, Makrostomie, Ohrenmißbildung, abstehende und tiefstehende Ohren auch gesondert erblich oder inmitten anderer Komplexe auftreten können. (S. und A. *W. Hallermann:* Vogelgesicht und angeborene Katarakt. – Klin. Mon. f. A. 1940, *113*. 4. 315). Hier liegt, besonders bei der Abgrenzung gegen andere craniale und craniofaciale Dysostosen noch ein wenig betretenes aber lohnendes Forschungsgebiet vor.

Nachschrift.

Während der Korrektur der Druckproben erscheint eine neue Arbeit von *A. Franceschetti* und *D. Klein:* The mandibular-facial Dysostosis, a new hereditary syndrome (Acta Ophth. 1949. 27. 2. 143), die das Weltschrifttum umfaßt und aus der wir entnehmen, daß noch einige erblich-familiäre Fälle beschrieben worden sind. Es sind diejenigen von *Debusmann*, 1940 (10 Personen durch 3 Generationen, teilweise komplett oder nahezu komplett, teilweise inkomplett, einmal von einer phänotypisch normalen Konduktorin übertragen, einmal in der extremen Form einer Otocephalie), von *Brohm* und *Kluska* (1940) bei Großmutter, Vater und Tochter mit intrafamiliärer Variabilität und von *Straith* und *Lewis* (1949) bei einer Mutter und 4 Kindern in typischer Form (Literatur siehe Franceschetti und Klein). Nach einer neuen Mitteilung von *Navis* (1949) teilt der Ohrenarzt *van Gilse* mit, daß er eine Frau mit gleichartiger Abweichung und totaler Atresie beider Gehörgänge sah, deren Vater eine leichtere Form derselben zeigte. Damit ist die Zahl der vererbten Fälle in den Niederlanden auf drei und die Anzahl aller beobachteten Fälle auf zehn erhöht.

Zusammenfassung.

Eine Beschreibung von acht niederländischen Fällen der seltenen Dysostosis mandibulofacialis, davon einer schon 1932 von *Waardenburg* entdeckt und veröffentlicht und vier erst 25 Jahre später selbstbeobachtete neue Fälle mit drei seitdem von anderen gefundenen und demonstrierten Fällen. Sie waren dreimal isoliert und kamen zweimal bei mehreren Familienmitgliedern vor (bei Vater, Sohn und Nichte, und bei Tochter und Mutter). Offenbar liegt ein unregelmäßig-dominanter Erbfehler vor mit schwacher und variierender Penetranz, gleich wie bei anderen frühembryonal sich auswirkenden Genen. Die formale Genese der Mißbildung läßt sich aus der normalen Ontogenese dadurch erklären, daß gegen Ende der 6. oder Anfang der 7. Embryonalwoche, wo das äußere Ohr und die Augenlider sich ausbilden, das polyphaene Gen beide Bezirke stört, nachdem zuerst im 1. Kiembogen eine primäre Dysplasie des Unterkiefers und des Jochbeines aufgetreten ist. Die meisten Symptome lassen sich also auf eine primäre Hemmungsmißbildung zurückführen, während andere auf reaktiver Hyperplasie in benachbarten Teilen oder, wie die merkwürdige embryonal normaliter nicht vorhandene Unterlidabknickung,

auf sekundären Ereignissen beruht. Noch im 3. bis Anfang des 4. Monats können Folgeerscheinungen auftreten. Die polymorphen Phaenotypen des Schrifttums entstehen dadurch, daß der Erbfehler sich mit individuellen Erbmerkmalen der getroffenen Organe verbindet. Aus weitern Beispielen geht hervor, daß Dysplasien des Unterkiefers, des Ohres, des Jochbeins und des Angesichts durch sehr verschiedene Ursachen in einer offenbar labilen kritischen frühen Entwicklungsperiode auftreten können.

Summary.

A description is given of eight Dutch cases of the rare Dysostosis mandibulofacialis, five of which examined by the author and three since added by others but demonstrated to the author. One of the cases was already described in 1932 but it was 25 years before new cases came. There were three sporadic and two familial cases (one in a father, son and niece, one in a daughter and her mother). The cause must be an irregularly-dominant gene, whose penetrance is feeble and which is very variable, giving rise to many minor cases. The defect manifests itself at the end of the 6th or the beginning of the 7th week of embryologic development. The authors try to explain and reconstruct the formal genesis of this anomaly by reviewing the ontogenesis of the normal human eye. Beginning with a dysplasia of the mandibula and the zygomatic bone and other anomalies of the first bronchial arch, it is by chance that the gene affects the eyelids and the outer ear at the same time of development. The syndrome can be explained by arrests of development, combined with reactive hyperplasia in adjoining tissues. The curious shape of the underlid is one of the secondary phenomena, some of which may not arise until the 4th month. Polymorphic phaenotypes in literature may be due to the interaction of the gene with individually inherited peculiarities. The authors mention very different causes for the development of the chief symptoms of the syndrome in an apparently labile critical early period of development.

Résumé.

Une description d'huit cas hollandais de la rare Dysostosis mandibulofacialis est donnée. Les auteurs ont recueilli cinq cas, les autres leur sont démontrés après. *Waardenburg* avait découvert et décrit un des cinq cas en 1932 et devait attendre pendant 25 années pour ren-

contrer d'autres. Trois fois les cas étaient isolés et deux fois ils étaient familiaux (père, fils et nièce; fille et sa mère). L'affection doit être héréditaire et transmise par un gène irregulièrement dominant avec une pénétrance faible et une expression très variable, parce qu'il y a beaucoup de formes frustes. Le défaut commence à paraître à la fin de la sixième et au commencement de la septième semaine embryonnaire. Les auteurs essaient de comprendre et de reconstruire la génèse de cette malformation à partir de l'ontogénèse de l'oeil humain normal. D'abord il y a un arrêt dans le premier arch branchial qui aboutit à une dysplasie de la mandibule et de l'os zygomatique et par hasard à une affection simultanée des paupières et de l'oreille, qui se trouvent dans le même stade de développement. On peut expliquer le syndrome en acceptant un arrêt de développement, combiné avec des hyperplasies conjointes et suivi d'anomalies secondaires comme la forme colobometeuse des paupières, pas présente dans l'ontogénèse et par d'autres malformations qui peuvent paraître jusqu'au commencement du quatrième mois. Le polymorphisme dans les cas de la littérature et causé par l'action combiné du gène et des traits hérités individuels. Les symptômes capitaux du syndrome peuvent être provoqué par des causes tout à fait différentes dans la periode évidemment labile et critique du premier développement embryonnaire.

LITERATUR

über Mißbildungen des Gesichts und der Augengegend.

Bishop, Harman: N. 1903. Trans. O.S.U.K. 23, 256. – *Dahlberg, G.:* 1926. Twin births and twins from a hereditary point of view. Stockholm. Tiden. – *Franceschetti, A.* et *P. Zwahlen:* 1944. Bull. de l'Ac. suisse des Sciences méd. *1*, 2, 60. – *Franceschetti, A.* et *M. Valerio:* 1945. Confinia Neurol. *VI*, 5, 255. – *Isakowitz, J.:* 1927. Klin. Mon. f. A. *78*, 509. – *Leopold, I. H.: Mahoney F.* and *Mabel Lee Price.* 1945 and 1946. Arch. of O. 34, 210 and Am. J. of O. 29, 5, 598. – *Liebenam, L.:* 1938. Z. f. Menschl. Vererb. u. Konstit.lehre *22*, 4, 373. – *Lloyd, Johnstone:* 1943. Brit. J. of O. 27. 21. – *Mann, I.:* 1943. Brit. J. of O. *2*, 7, 13. – *Navis, H.:* 1947. Ned. Tydschr. voor Gen. *92*, 10, 740 und *93*, 33, 2852. – *Pfannmüller:* 1894. Zu den Kolobomen des Auges. Inaug. Diss. Gießen. – *Pirés de Lima, J. A.* und *Monteiro, H. B.*: 1923. Arg. de Anat. e Antrop. 8, 185. – *Hallermann, W.*: 1940. Klin. Mon. f. A. *113*, 4, 315. – *Rochat, G. F. Jr.:* 1936. Ned. Tijdsch v. Geneesk. *80*, 21, 2401. – *Sanvenero-Roselli, G.*: a) 1940. Plastica chirurgica (Milan) *1*, 184; b) 1948. Dtsch. zahnärztl. Z. *3*, 816. – *Schachter, M.:* 1947. Ann. pédiatr. *169*, 5. – *Strupler, W.:* 1947. Arch. Jul. Klausstift. *22*, 3/4, 169. – *Stupka, W.:* 1938. Die Mißbildungen und Anomalien der Nase und des Nasenrachenraums. Springer. Wien. – *Waardenburg, P. J.:* 1930. Gräfes Arch. *124*, 2, 221. – *Waar-*

denburg, P. J.: 1932. Ned. Tijdschr. v. Geneesk. *46*, 48, 5509. – 1932. Das menschl. Auge u. seine Erbanlagen. S. 51. – *Waardenburg, P. J.:* 1934. Klin. Mon. f. A. *92*, 29. – *Waardenburg, P. J.:* 1948. Ned. Tijdschr. v. Geneesk. *92*, 43, 3455. – *Zwahlen, P.:* 1944. Un Syndrome nouveau: La dysostose mandibulofaciale. Thèse de Genève. – *Zumsteeg, H.:* 1899. Drei Fälle von Kolobom der oberen Augenlider. Inaug. Diss. Tübingen.

Sammelreferate mit Literaturverzeichnis.

Dysostosis mandibulo-facialis: s. Franceschetti und *Zwahlen.* Erbliche Ohrenabweichungen s. *van Gilse, P. H. G., A. B. Hinnen* und *A. C. Nieuwenhuyse,* 1942. Heredity in the Field of Oto-Rhino-Laryngology. Bibliogr. Genetica 13, 4, 301 und *Albrecht, W.*, 1940. Erbbiologie und Erbpathologie des Ohres und der oberen Luftwege. Handb. d. Erbbiologie des Menschen. Bd. IV, 2, S. 4. – *Erbliche normale Variationen des Ohres:* 1. *Loeffler, L.*, 1940. Anwendungen der menschlichen Erbbiologie. Handb. d. Erbbiologie des Menschen, Bd. II. S. 330 und *Weniger, J.* Die anthropologischen Methoden der menschlichen Erbforschung daselbst, S. 22. – *Embryonale Entwicklung* s. *Broman, I.*, 1911. Normale und abnorme Entwicklung des Menschen. Bergmann. Wiesbaden; *van Duyse, M.*, 1905. Eléments de Tératologie de l'oeil. Encycl. franç. d'Ophth., Bd. II, 267. Colobome palpébrale etc. 497. *van Duyse, M.*, 1905. Embryologie de l'oeil. Ibid. 143–265. – *Ida Mann*, 1937. Developmental Abnormalities of the eye. Cambridge Univ. Press. – *Ch. Dejean* und *F. Granel-Montpellier*, 1947. Embryologie de l'oeil des vertèbres. Tabulae Biologicae Vol. 32, I, 154–165.

AN ATTEMPT TO DIFFERENTIATE BETWEEN HOMOZYGOTES AND HETEROZYGOTES OF THE ABO-SYSTEM BY EXAMINING THE SPERMATOZOA

by HJALMAR SJÖVALL
Stockholm

On account of their simple Mendelian mechanism the blood groups have commonly been accepted as legally binding proofs in paternity cases, when exclusion is in question. Their practical value is diminished, however, because such an exclusion is possible only in a certain percentage, the size of which depends on the distribution of genes over the whole population. Thus, the following figures, calculated on the distribution of phenotypes and genes given by *Wolff*, 1946 (Tab. 1), apply for Sweden.

Table 1. Distribution in the population of Sweden. (*Wolff* 1946).

Phenotype	%		Gene	Frequency	
A_1	36,800	47,350	A_1	$a_1 = 0{,}22756$	$a = 0{,}30815$
A_2	10,550		A_2	$a_2 = 0{,}08059$	
B	10,050		B	$b = 0{,}07764$	
O	37,725		O	$o = 0{,}61421$	
A_1B	3,450	4,875			
A_2B	1,425				

In its original form the ABO-system makes it possible to exclude 14,8%, calculated with a man taken at random in the population.

When the A-genes are divided into groups A_1 and A_2 this frequency is increased to 18.1%.

To this percentage must be added exclusions according to the MN-system and as regards the Rh factor, and possibly other factors, too. These factors are quite independent of the ABO-system, however, and will not be discussed below.

When calculating the above figures only the determination of phenotypes has been taken into account. If the genotype of the persons in question could also be found out, it would be possible to increase the percentage of exclusion. (On the other hand, no improvement is possible within the MN-system where the phenotype always expresses the genotype except in the case of the extremely rare gene N_2). Such a possibility, already employed in practice, is to be found in the investigation of ascendency and descendency. Binding proofs can, however, only be obtained by investigating the paternal and maternal grandmothers (pater semper incertus). Even if these persons are still alive and available for investigation, the results lead to conclusions in only a few cases.

The author has tried to find another way of approaching the problem:

As we know, group-specific agglutinogens and agglutinins are present in cells and fluids in the body other than the blood, as also in secretions and excretions. Their concentration is said to vary within different organs and tissues, and as regards secretions, individuals may be divided into secretors and non-secretors. Working with the spermatozoa *Landsteiner* and *Levine* (1926) showed that group-specific immune sera could be deprived of their agglutinins by absorption with living sperm cells. Various authors have subsequently confirmed these findings, and shown that agglutinogen is also present in the cell-free sperm plasma, and that it can be demonstrated in old sperm stains. Recent investigations, finally, show that, as regards secretion, the sperm behaves in the same way as the saliva (*Fukao*, 1939, and *Kikkawa*, 1939).

The spermatozoa differ from the other cells of the body, however, by their single set of genes; in heterozygotes two different kinds of spermatozoa are obtained (50% R and 50% r). The author's idea was that it might be possible to prove this difference by means of group-specific reactions.

Tables 2 and 3 give a survey of the new possibilities of exclusion which might be obtained by a knowledge of the genotype of the alleged father. It is, of course, impossible to determine the genotype of mother and child with this technique.

According to the ABO-system the chances of exclusion (without division into A_1 and A_2) increase from 14.8 to 19.4% and the chances of exclusion according to the A_1A_2BO-system from 18.1 to 24.4% when applied on the distribution of genes in Sweden.

Table 2. Exclusions according to ABO-system.

a) Phenotype combinations of mother and child. Men excluded as fathers (genotype).

Mother / Child	A	B	O	AB
A +	BB	Without A		BB
A —				
B +	Without B	AA	Without B	AA
B —				
O +	Without O			×
O —	AB			
AB +	Without B	Without A	×	OO
AB —				

+ = Exclusions with diagnosis of male heterozygotisme.
— = Exclusions without diagnosis of male heterozygotisme.
× = Impossible combinations.

The author has performed a series of investigations on human sperm, in an attempt to ascertain the supposed differences [1]).

A preliminary experiment showed that a fractionated agglutination can be made. If A-blood corpuscles and B-blood corpuscles are mixed, a partial agglutination can be obtained with α- or β-serum, and the agglutination then becomes complete, if the remaining serum is added.

As mentioned above, we know that both spermatozoa and sperm plasma in secretors contain specific agglutinogens and this has also been ascertained on the sperm samples from group A, in our material. One case of 11 was found to be a non-secretor. Experiments to prove agglutinins in the sperm were negative, however: No certain agglutination of the added A- and B-corpuscles respectively was

[1]) The author wants to express his very great gratitude to professor *Erik Wolff* for the opportunity to make his experiments at Statens rättskemiska laboratorium, Stockholm.

Table 2. b) Expected frequency of exclusions.

Type of exclusion (genotype of excluded man)	Frequency of combinations of mother and child in the population	×	Frequency of men (in the population) possible to exclude	Actual figures for Sweden Without diagnosis of male heterozygotisme	Actual figures for Sweden With diagnosis of male heterozygotisme
+, — Without A	$a(1-a)^2$	×	$(1-a)^2$	0,0706	0,0706
+, — Without B	$b(1-b)^2$	×	$(1-b)^2$	0,0562	0,0562
+ Without O	o^2	×	$(1-o)^2$		0,0562
— AB		×	2 ab	0,0181	
+ AA	$b(b+bo+o)$	×	a^2		0,0055
+ BB	$a(a+ao+o)$	×	b^2		0,0021
+, — OO	$ab(1-o)$	×	o^2	0,0035	0,0035
			Total	14,84%	19,41%

+ = with diagnosis of male heterozygotisme.
— = without diagnosis of male heterozygotisme.

obtained. But this is of no importance in the present connection, as it is scarcely probable that the O-spermatozoa in heterozygotes should form agglutinins, which in that case should be active against the specific cells of the body. (Control experiments showed – as was expected – that O-sperm did not absorb any agglutinin and that A-sperm did not absorb α-agglutinin.)

Experiments aiming at specific agglutination of spermatozoa are disturbed by the spontaneous agglutination of the spermatozoa which takes place normally, and often very markedly, in fresh samples. Such a spontaneous agglutination was found to occur with O-spermatozoa and A-spermatozoa alike, both in their own plasma and in suspension of the spermatozoa in physiological salt solution and in A- and B-serum respectively. These agglutinates can be dissolved again by shaking or stirring. The agglutination ceases with the mobility of the spermatozoa. It is of different strength in the different sperm samples. In one sample, where even the fresh sample showed poor mobility and only contained 26 million sperma-

Table 3. Exclusions according to A_1A_2BO-system.

a) Phenotype combinations of mother and child. Men excluded as fathers (genotype).

Child \ Mother		A_1	A_2	B	O	A_1B	A_2B
A_1	+	BB	Without A_1			BB	Without A_1
	—						
A_2	+	$(A_1+B)^2$	Without A_2			×	$(A_1+B)^2$
	—	A_1B	BB BO OO A_1B				A_1B
B	+	Without B	$(A_1+A_2)^2$	Without B		$(A_1+A_2)^2$	
	—						
O	+	Without O				×	
	—	A_1B A_2B					
A_1B	+	Without B	×	Without A_1	×	$(A_2+O)^2$	Without A_1
	—						
A_2B	+	Without B		Without A_2	×	Without A_2	$(A_1+O)^2$
	—			BB BO OO A_1B		BB BO OO A_1B	OO

Signs like $(A_1 + B)^2$ mean: A_1A_1 and BB and A_1B.
+ = Exclusions with diagnosis of male heterozygotisme.
— = Exclusions without diagnosis of male heterozygotisme.
× = Impossible combinations.

tozoa/cm³, and where the spermatozoa in the untreated sample already showed numerous abnormal shapes (large, small, free tails, great protoplasmic heads), no spontaneous agglutination at all could be obtained.

Thus, no difference in agglutination which might be interpreted as group-specific could be obtained with the mobile spermatozoa. In older samples, where the mobility had ceased, no agglutination at all, group-specific or otherwise, could be obtained.

Table 3. b) Expected frequency of exclusions.

Type of exclusion (genotype of excluded man)	Frequency of combinations of mother and child in the population	×	Frequency of men (in the population) possible to exclude	Actual figures for Swedes: Without diagnosis of male heterozygotisme	With diagnosis of male heterozygotisme
+/— Without A_1	$a_1 (1 - a_1)^2$	×	$(1 - a_1)^2$	0,0810	0,0810
+ Without A_2	$a_2 [(b+o)^2+a_1b]$	×	$(1 - a_2)^2$		0,0338
— BB BO OO A_1B		×	$(b+o)^2 + 2a_1b$	0,0206	
+/— Without B	$b (1 - b)^2$	×	$(1 - b)^2$	0,0562	0,0562
+ Without O	o^2	×	$(1 - o)^2$		0,0562
— A_1B A_2B		×	$2b (a_1+a_2)$	0,0181	
+ $(A_1+A_2)^2$	$b (b+bo+o)$	×	$(a_1+a_2)^2$		0,0055
+ BB	$a_1 (a_1+a_1a_2+a_2+a_1o+o)$	×	b^2		0,0015
+ $(A_1+B)^2$	$a_2 (a_2+a_1o+a_2o+o)$	×	$(a_1+b)^2$		0,0066
— A_1B		×	$2a_1b$	0,0025	
+ $(A_1+O)^2$	$a_2b (a_2+b)$	×	$(a_1+o)^2$		0,0007
— OO		×	o^2	0,0004	
+/— $(A_2+O)^2$	$a_1b (a_1+b)$	×	$(a_2+o)^2$	0,0026	0,0026
			Total	18,14%	24,41%

Signs like $(A_1+B)^2$ mean: A_1A_1 and BB and A_1B.
+ = Exclusions with diagnosis of male heterozygotisme.
— = Exclusions without diagnosis of male heterozygotisme.

For this reason experiments were made with a haemolytic serum. This showed a nearly complete agglutination inhibition for both A_1 and A_2 and B-blood corpuscles, and complete haemolysis of such blood corpuscles after 24 hours at 37° C. Washed spermatozoa from several different sperm samples (belonging to group O and A respectively) were added to this serum. After 24 hours at 37° sediment was observed in all the samples. They could easily be suspended and, when examined microscopically, they were found to consist of unchanged spermatozoa. If any of the A-samples had belonged to a homozygote and if a spermiolysis had been possible, it would, of course, have taken place. If, on the other hand, all the samples, had belonged to heterozygotes, there is still a possibility that 50%

had been dissolved, while the remaining half had remained unaffected. Therefore the experiment was repeated quantitatively and the number of spermatozoa counted before and after the incubation. No statistically significant differences could be ascertained.

This investigation has given negative results. The reason for publishing it is firstly that negative results also are of interest, secondly that another research worker could get the same idea. This is to prevent him from some unnecessary work.

Summary.

The author thought it might be possible to prove differences between homozygotes and heterozygotes of the ABO-system by group-specific reactions on the spermatozoa (which after the reduction-division have a different set of genes). Such differences could not be proved either with agglutinating or with haemolyzing sera (on a material of 11 samples of human sperm).

Résumé.

L'auteur pensait qu'il serait possible de prouver la différence existant entre les homozygotes et les hétérozygotes dans le système ABO en se basant sur des réactions spécifiques présentes dans certains groupes de spermatozoïdes (qui ont une composition génotypique différente après réduction-division). Ces différences ne purent être mises en évidence, ni par des sera agglutinants, ni par des sera hémolysants (expérience faite avec 11 échantillons de sperme humain).

Zusammenfassung.

Es war die Auffassung des Verfassers, daß es möglich sein müßte, Unterschiede zwischen Homozygoten und Heterozygoten des ABO-systemes an gruppen-spezifischen Reaktionen der Spermatozoen (die nach Reduktionsteilung verschiedene Genen haben können) zu zeigen. Derartige Unterschiede konnten weder durch Agglutination noch durch Hämolyse der Sera gezeigt werden. (Das Material umfaßte elf Proben menschlicher Spermen).

LITERATURE

Fukao, T.: Jap. J. M. Sc. VII Soc. Med. and Hyg. *3*, 1939. – *Kikkawa, K.:* Jap. J. M. Sc. VII Soc. Med. and Hyg. *3*, 1939. – *Landsteiner, K.* and *P. Levine:* J. of Immun. *12*, 1926. – *Wolff, E.:* Statens offentliga utredningar nr 49, 1946 (Swedish).

From the University Institute of Human Genetics, Copenhagen
Head: Professor Tage Kemp, M. D.

ANTHROPOLOGICAL MEASUREMENTS OF GREENLANDERS IN THE SOUTHERN DISTRICT OF JULIANEHAAB

by VIBEKE FABRICIUS-HANSEN

The population of West Greenland consists mainly of a mixture of Eskimos and Europeans. The origin of the Eskimos (5, 16, 23, 12, 21) has been a topic widely discussed since *Cranz* in 1770 formed the theory that physically and linguistically they were related to the Mongoles in Central Asia (the Kalmucks). Another theory (*Boyd Dawkins*) in 1874 claims that the Eskimos are descendants of the palaeolithic cave dwellers of Europe, who followed the reindeer northwards when the ice disappeared. *Rink*, *Boas*, *Steensby* (23) and others are of the opinion that the Eskimos originally were an inland people originating from North America. Following the rivers they have come down to the coasts and have there developed a culture suited to the arctic conditions and special living opportunities.

According to the first theory which seems to be widely accepted the Eskimo migrated from the north eastern Siberia across the Berings Street and finally spread to their present extended domains. As far as is known the Eskimos reached Greenland via Smith Sound before the year 982 after having settled in the northermost parts of North America. In the course of centuries they have moved down along the west coast of Greenland, where towards the end of the 12th century they met the Norsemen.

The historic sources seem to show that the Eskimos first came to the southern part of Greenland (called Østerbygden) towards the end of the 14th century and destroyed the Norsemen's settlements there. Whether any mixture of blood between the two peoples has taken place is unknown (2, 3, 10). Part of the Eskimos continued their wanderings around to the east coast.

Later, probably during the first half of the 17th century, the whalers began to sail along the Greenland coasts. They carried on

extensive commerce with the Eskimos and have supposedly mixed with them (24). It has been reported that entire Eskimo families were captured and brought to Europe as curiosities.

Possibly the Eskimo population might have been partly destroyed by the reckless treatment of the whalers. However, in the year of 1721 *Hans Egede* came to South Greenland and founded the Danish colonization. As years passed a great number of Danish officials have arrived in Greenland through the establishment of commercial and missionary stations, and gradually a more or less mixed population has arisen. Only in the most southern districts in the regions around Cape Farewell rather unmixed groups of Eskimos are living. This is due to the fact that part of the Eskimos that migrated to the southern east coast during the 19th century again returned to the southern west coast, as in this way they came closer to the Danish commercial stations and had less difficulties to procure their necessities.

As access to this part of Greenland is difficult due to the special ice conditions here, the abovementioned group of Eskimos has been living a more isolated existence than the population of the northern latitudes of the west coast and has thus preserved its unmixed character. The last heathen east coast Eskimos migrated to the west coast during the late summer of 1900 (3).

In the summer of 1939, aided by a grant of the Carlsberg Foundation and with the permission of the Greenland Government, I have taken anthropological measurements of part of the population in the southern district of Julianehaab.

Only after the war I have received my notes and had the opportunity of analysing these. I have closely followed the instructions I have received, and I have registered all measurements and observations together with the conditions under which the measurements were made.

The measurements were made during a journey from Julianehaab to Nanortalik, and from there southwards to dwelling places and outposts around Cape Farewell.

Longer stays were made in Julianehaab and Nanortalik, where I got permission to use the school for my measurings. From there I went further south by motorboat to Nunarssuit, Ikigait, Igdlokasik, Frederiksdal, Pamiagdluk, Itivdleq, Augpilagtoq and Sangmissok.

My material comprises 272 persons of which 130 are males and 142 are females, divided in the following age-classes.

Table 1.

Age	Males	Females
17–20 years	18	21
20–29 years	63	57
30–39 years	21	27
40 years and over	28	37

The result of my observations regarding the weight of the examined Greenlanders is shown by the following table. The state of nourishment was generally good.

Table 2.

Weight	Males	Females
–40 kilos	0	1
40–49 kilos	6	29
50–59 kilos	35	67
60–69 kilos	68	30
69 and over	12	3

121 of the males have been weighed. The weights range between 42–77 kilos, 55,7% between 60–69 kilos. 130 of the females have been weighed. The weights range between 39–82 kilos, 51,5% between 50–59 kilos. The persons were weighed fully dressed but without footwear.

The Greenlanders make on an average a plump impression, and their fat is evenly distributed on body and limbs, while their cheeks generally are especially round.

The state of health among those examined was apparently good, but any medical examination was not undertaken. Nobody, however, showed symptoms of any acute diseases. The structure of their muscles is well developed, and they are wellknown for their physical endurance.

The face is oval or pentagonal often with protuding cheekbones, which as mentioned creates a more full appearance. The face is strikingly flat, the nose slightly prominent, the mouth rather big.

No tatoos were found.

The hair of the head is generally abundant. Among the 130 males (28 over 40 years) only one was found baldheaded. The color of the hair is almost black among all females and males, very few (a total of 3) had brown-black hair and one individual brown hair. Even up to a high age the hair keeps its black color. Only two males were found greyhaired, 18 were grizzled, among the females 16 were found to be grizzled.

The hair of all the 130 males was quite smooth, among the females 6 had curly or wavy hair, the rest had smooth hair. The hair of the body is sparse. Only 55.4% of the males had axillary hair and of the females only 47.2%. The pubic hair was not examined.

Beard was missing in 8.5% of the males and very sparse in 37.7%, while 50.8% had straggling hairs on the upper lip and chin. Among the females 12.6% had powerful downs on the upper lip.

The color of the skin on the inner side of the upper arm has been determined with the aid of *Bruno-Schultz*'s color chart. The color chart, however, does not present the correct color shades. The skin is often rather fair or like a tanned nordic skin. The skin of the face is considerably darker, strongly brown or cupper colored in the males in summer, when they stay out in the strong light all day long.

Table 3.

Color shade of the skin	Males	Females
3	2	0
4	2	2
5	6	12
6	14	27
7	71	88
8	20	12
9	12	0
10	3	1

The color of the eyes is likewise measured by *Bruno-Schultz*'s color chart.

Table 4.

Color shade of the eyes	Males	Females
7	2	2
8	4	2
9	1	0
10	5	2
11	7	4
12	4	4
13	19	13
14	37	52
15	42	61
16	9	2

The eyeslit is slanting in 32.3% males and 37.2% females, otherwise straight. It is considerably narrower than among Europeans: among 45.4% males and 43% females it is especially narrow, while only 5.4% males and 8.4% females had a wide eyeslit i. e. corresponding to that of a European.

The so-called mongoloid eyefold (plica nasopalpebralis superior) was found in 21.6% of the males, especially pronounced among 7.7%, and in 25.6% and 5.6% of the females respectively. The eyelidfold (sulcus orbitalis superior), which often disappears on account of the strongly developed lay of fat around the eyes, was present among 45.4% males and 27.5% females. The forehead was especially steep among 21.5% males and 35.2% females, while among 4.6% males and 1.4% females it was strikingly slanting. The slants of the forehead of the rest were placed between these extremes, but were on an average more steep than those of the Scandinavians.

In 46.2% males and in 52.8% females the nose was straight, in 29.2% males and 14.1% females curved and in 24.6% males and 33.1% females flat.

The mouth is on an average big, and the lips, especially the lower lip, full.

The ears were as a rule small and wellshaped, but the lobe was rudimentary in a great amount of cases, namely in 67.7% males and 78.9% females.

The teeth were generally good, but some had very much worn teeth (27.7% males and 22.5% females).

The anthropological measurements were undertaken with *R. Martin*'s anthropometrical set. Before the departure I had finished a course in Anthropometry with Dr. *Lester* at the Musée de l'Homme in Paris, where I had the opportunity to make practical measurements. My interest was aroused by Dr. *R. Gessain*, who during 1934–1935 had made similar anthropological measurements in Angmagssalik, and it was my intention to correlate my results with his – so far they have not been published.

The anthropological measurements were difficult to perform in the rather primitive conditions available. The rooms at my disposal were rather chilly, or the measurements had to be taken in the open air, and it was often difficult to make these primitive people keep still during the examination.

These and many other circumstances may possibly have caused the measurements to be slightly incorrect, which, however, one should keep in mind is the case in all anthropological measurements on living individuals.

The measures that have been analysed in the present work is seen

Table 5.

Measurement	Number	Min.	Max.	Mean
Males				
Stature, cm	128	138.5	177.0	159.3
Length of trunk, cm	129	36.1	57.7	47.7
Height of acromion, cm	129	111.3	143.1	129.4
Height of spina iliaca ant. sup., cm	127	73.3	99.6	88.5
Span, cm	128	140.5	174.7	160.1
Sitting height, cm	130	71.1	93.2	85.4
Diameter biacromialis, cm	130	30.1	41.0	36.8
Diameter bicristalis, cm	130	20.5	30.7	27.9
Antero-posterior measure of the chest, cm	129	17.5	23.7	20.1
Circumference of the chest, cm	127	77.3	103.7	92.0
Circumference of the head, cm	126	52.9	60.2	56.5
Greatest head-length, cm	130	17.5	20.5	19.31
Greatest head-width, cm	128	14.0	16.5	15.22
Cheekbonewidth, cm	128	13.2	16.2	14.57
Morphological facial length, cm	126	11.0	14.5	12.77
Cephalic index	130	.	.	78.9
Females				
Stature, cm	142	133.0	161.3	150.1
Length of trunk, cm	138	39.0	50.8	45.5
Height of acromion, cm	142	103.7	131.3	121.8
Height of spina iliaca ant. sup., cm	139	70.9	91.0	82.8
Span, cm	142	128.5	164.5	149.7
Sitting height, cm	141	71.7	88.2	82.8
Diameter biacromialis, cm	137	30.7	38.3	33.9
Diameter bicristalis, cm	140	23,5	31.3	28.1
Antero-posterior measure of the chest, cm	141	14.7	22.2	18.4
Circumference of the chest, cm	139	76.6	99.5	87.3
Circumference of the head, cm	140	52.2	58.8	55.2
Greatest head-length, cm	142	17.1	20.4	18.70
Greatest head-width, cm	142	13.3	16.0	14.70
Cheekbonewidth, cm	141	12.7	15.1	13.91
Morphological facial length, cm	141	10.3	13.5	12.13
Cephalic index	142	.	.	78.7

from table 5. They have all been taken according to *R. Martin* (15), except the sitting height, the antero-posterior measure of the chest and the circumference of the chest.

The sitting height is measured on the sitting individuals from vertex cranii to the seat.

The antero-posterior measure of the chest is the distance between sternum at the level of the processus xiphoideus and the processus spinosus columnae dorsalis on the same horizontal plane measured midway between extreme inhalation and extreme exhalation.

The circumference of the chest is the greatest circumference of the thorax in its middle position between in- and exhalation.

When describing an anthropological material like this you generally calculate the arithmetical mean, the standard error of the mean and the standard deviation. In this way it will be possible to make a comparison between two groups.

When using such intermarried groups of people there is a risk of finding differences which are due only to family selection and has nothing to do with racial differences. The distributions of the various measurements are given in the appendix tables I–V, the arithmetical means, the minimum and maximum values are given in table 5. It must again be emphasized, that we are not certain about these means being at all characteristic of the group in question and far less about their distributional laws. Therefore the standard deviations are not calculated.

It appears that some of the persons (a total of 8) were measured in 1935 by *Dr. Fischer-Møller* (8). The comparison between the two sets of measurements shows that as regards some few measures a systematic deviation apparently exists between the measurements, expressing the lack of exactness which may be expected when making such anthropological measurements of living persons „in the field".

Anthropological measurements on living Eskimos and Greenlanders have formerly been taken by Søren Hansen 1893 and 1914 (10, 11), *K. Poulsen* 1909 (20), *Fischer-Møller* 1935 (8) and by *R. Gessain* in 1935 (9).

As far as the Canadian Eskimos are concerned measurements have been published from the southern part of Baffin Land (22), Labrador (25, 19, 26) and from the Cupper Eskimos (13) (around Coronation Gulf), these groups are most closely located and probably most closely related to the population of Greenland, provided it is taken for granted that the Eskimos migrated to Greenland from North America via Smith Sound.

Comparing earlier examinations with mine, the following data (table 6) are found:

Table 6.

		Stature	Head-length	Head-width	Cephalic index	Facial length	Cheek-bone-width
Soren Hansen (10)	(546 M)	162.0	19.21	14.85	77.3	12.37	14.13
West Greenland 1893	(474 F)	152.0	18.61	14.23	76.8		
Soren Hansen (11)	(53 M)	162.9			76.9		
East Greenland 1914	(38 F)	153.8			75.6		
K. Poulsen (20)	(29 M)	161.1	19.2	14.7	76.5		
East Greenland 1909	(11 F)	147.7	18.4	14.0			
Gessain (9)	(113 M)	162.4	19.37	14.74	76.2	12.30	14.47
East Greenland 1935	(137 F)	152.6	18.61	14.21	76.4	11.43	13.89
The present author	(130 M)	159.3	19.31	15.22	78.9	12.77	14.57
South-West Greenl.	(142 F)	150.1	18.70	14.70	78.7	12.13	13.91
Birket-Smith (4)	(113 M)	160.6	19.29	14.90	77.3	12.31	14.26
Hudson Bay 1940							
Jenness, 1923 (13)	(82 M)	164.8	19.59	15.18	77.6	12.69	14.57
Coronation Gulf	(65 F)		19.57	15.11	77.3	12.77	14.71
Cumberland Sound (22)	(21 M)	158.5					
Labrador (25)	(37 M)	157.0	19.29	15.15	78.6		
Labrador (19)	(11 M)	157.7					
Labrador (26)	(58 M)	158.3	19.22	14.83	77.3		

The stature of the individuals as measured by me is about 2 cm. lower than shown by *Søren Hansen* in his extensive work (1020 individuals). It cannot be said with certainty whether he has measured the persons without footwear, or whether he, as *Birket-Smith* did, has deducted some millimeters. Besides he has only measured persons over 20 years of age, and he calls special attention to the fact that the general growth (of stature) cannot be considered complete until somewhere in the thirties.

The state of nourishment and general living conditions are undoubtedly far better in West Greenland now than 50 years ago, and the European admixture is now hardly smaller than at that time (however in the district of Julianehaab in 1928 it was estimated to be only 12%), but it does not seem that these facts have affected the growth of stature.

The East Greenlanders (9, 20) are found to be slightly taller than the South-West Greenlanders, who are of about the same height as the Hudson Bay Eskimos (4), and slightly taller than the Labrador Eskimos (25, 19, 26). The Cupper Eskimos (13), however, are about

5 cm. taller. There is hardly any reason to suppose that the short stature of the South-West Greenlanders should have been caused by a degeneration as a consequence of the European admixture. It may be possible, though, that the low stature is a dominant feature among the Eskimos.

The cephalic indexes of the various groups indicate a fairly good agreement, as on the southern west coast *Søren Hansen* (10) finds the index of males 78.1 of females 76.8, while the larger group of West Greenlanders has a somewhat lower index (77.9 and 76.4). On the East Greenlanders (9, 20) indexes are even lower, but still within the same group: mesocephalic. The Hudson Bay (4) and Cupper Eskimos (13) have about the same cephalic index, while the Labrador group (25, 19, 26) shows an increasing tendency.

The index is constantly rising, when from Coronation Gulf you go further west, and attains its culmination with a value of 81.4 in the Colville Eskimos (22), who are bradycephalic.

The figures for morphological facial length and cheek-bonewidth do not diverge materially among the various groups.

Table 7.

		Length of trunk	Height of acromion	Height of spin. il. ant. sup.	Span	Sitting-height	Diam. biacr.
Birket-Smith Hudson Bay 1940	(113 M)	48.6	—	—	—	—	—
Gessain	(113 M)	—	132.2	90.0	165.1	89.2	36.5
East Greenland 1935	(137 F)	—	124.2	83.6	153.6	85.7	33.2
The present author	(130 M)	47.7	129.4	88.5	160.1	85.4	36.8
South-West Greenland	(142 F)	45.5	121.8	82.8	149.7	81.7	33.8

		Diam. bicrist.	Antero-posterior measure of the chest
Birket-Smith Hudson Bay 1940	(113 M)	—	—
Gessain	(113 M)	28.8	23.2
East Greenland 1935	(137 F)	29.2	21.4
The present author	(130 M)	27.9	20.1
South-West Greenland	(142 F)	28.2	18.4

Table I.

Distribution of stature, length of trunk and height of acromion.

Stature				Length of trunk			Height of acromion			
cm	M	cm	F	cm	M	F	cm	M	cm	F
		131–134	1	36–37	2				101–104	1
		134–137	1	37–38	—				104–107	
138–141	3	137–140	6	38–39	—				107–110	2
141–144	1	140–143	11	39–40	—	1	111–114	3	110–113	7
144–147	3	143–146	12	40–41	1	3	114–117	3	113–116	8
147–150	4	146–149	25	41–42	1	4	117–120	2	116–119	21
150–153	8	149–152	31	42–43	3	9	120–123	10	119–122	25
153–156	16	152–155	27	43–44	4	21	123–126	15	122–125	36
156–159	23	155–158	20	44–45	15	21	126–129	22	125–128	32
159–162	26	158–161	7	45–46	5	21	129–132	23	128–131	7
162–165	20	161–164	2	46–47	14	25	132–135	31	131–134	3
165–168	17			47–48	15	14	135–138	16		
168–171	4			48–49	24	10	138–141	1		
171–174	2			49–50	20	7	141–144	3		
174–177	1			50–51	11	2				
				51–52	10					
				52–53	3					
				53–54	—					
				54–55	—					
				55–56	—					
				56–57	—					
				57–58	1					

The rest of my anthropological measurements, which have been analysed, correspond well to the measurements of *Gessain* (9) in East Greenland.

Only the following few conclusions can be drawn from this examination:

The group of people in South-West Greenland examined by me consists partly of supposedly unmixed Eskimos, partly of such with a more or less European admixture.

Attempts to demonstrate a real difference between these two groups have failed, wherefore the group has been treated as a unity.

It cannot be shown that the European admixture has had any material influence on the anthropological measurements within the

Table II.

Distribution of height of spina iliaca ant. sup., the span and the sitting height.

Height of spina iliaca ant. sup.			Span				Sitting height			
cm	M	F	cm	M	cm	F	cm	M	cm	F
70– 72		1			127–130	1	71–74	1	70–73	1
72– 74	1	2			130–133	—	74–77	4	73–76	9
74– 76	1	3			133–136	1	77–80	8	76–79	18
76– 78	2	7			136–139	8	80–83	22	79–82	43
78– 80	4	18	140–143	3	139–142	9	83–86	30	82–85	50
80– 82	2	27	143–146	1	142–145	11	86–89	46	85–88	18
82– 84	6	20	146–149	4	145–148	25	89–92	15	88–91	2
84– 86	14	24	149–152	7	148–151	24	92–95	4		
86– 88	25	25	152–155	12	151–154	26				
88– 90	21	10	155–158	21	154–157	22				
90– 92	25	2	158–161	21	157–160	9				
92– 94	16		161–164	23	160–163	3				
94– 96	6		164–167	16	163–166	3				
96– 98	2		167–170	12						
98–100	2		170–173	4						
			173–176	4						

South-West Greenland population. The stature is thus lower than that of the pure Eskimo group on the east coast, while the cephalic index is larger, placed nearer bradycephalic values.

Summary.

An anthropological examination has been made during the summer 1939 on part of the population of the south western coast of Greenland. Earlier theories on the origin of the population are quoted, and the special living conditions shortly described.

The group of the population which has been examined consists partly of unmixed Eskimos, partly of such with more or less admixture of European blood.

The material comprises 130 males and 142 females. A general characteristic of their appearance is given, and anthropological measurements have been made with *R. Martins* anthropometric set. The result of the measurements is given in table 5 and tables I, II and III.

Table III.

Distribution of diameter biacromialis, diameter bicristalis and the antero-posterior measure of the chest.

Diameter biacromialis			Diameter bicristalis			Antero-posterior measure of the chest		
cm	M	F	cm	M	F	cm	M	F
30–31	1	4	20–21	1		14–15		2
31–32	1	15	21–22	—		15–16		5
32–33	1	25	22–23	—		16–17		19
33–34	6	29	23–24	1	1	17–18	10	31
34–35	12	30	24–25	3	3	18–19	28	39
35–36	22	28	25–26	8	4	19–20	25	30
36–37	28	4	26–27	20	18	20–21	30	10
37–38	26	1	27–28	39	38	21–22	22	4
38–39	18	1	28–29	25	43	22–23	11	1
39–40	13		29–30	28	21	23–24	3	
40–41	2		30–31	5	10			
			31–32		2			

Comparisons with earlier authors show good agreement. It cannot be proved that the European admixture has had any essential influence on the anthropological measurements of the South-Western Greenlanders.

Résumé.

Les recherches anthropologiques en question d'une partie de la population, habitant à la côte sud-ouest du Groenland, ont été faites en été 1939. On a mentionné les théories qui existent sur la provenance de cette population et les conditions particulières de la vie étaient décrites brièvement.

Le groupe de la population qu'on a examiné consiste d'une part d'Esquimaux tout à fait purs, et d'autre part d'Esquimaux-métis qui ont le sang mêlé à l'européen dans une proportion plus ou moins grande.

La totalité du nombre d'individus comprend 130 hommes et 142 femmes. On a décrit le caractère général du phénotype, basé sur les

Table IV.

Distribution of circumference of the chest, circumference of the head and the greatest head-length.

Circumference of the chest				Circumference of the head			Greatest head-length		
cm	cm	cm	F	cm	M	F	mm	M	F
76– 78	1	75– 77	1	52–53	3	6	170–172	0	1
78– 80	—	77– 79	5	53–54	3	20	172–174	0	1
80– 82	2	79– 81	6	54–55	15	51	174–176	1	1
82– 84	3	81– 83	11	55–56	26	29	176–178	—	5
84– 86	6	83– 85	25	56–57	35	19	178–180	1	7
86– 88	13	85– 87	16	57–58	25	13	180–182	2	10
88– 90	20	87– 89	31	58–59	14	2	182–184	4	14
90– 92	18	89– 91	16	59–60	4		184–186	7	22
92– 94	23	91– 93	11	60–61	1		186–188	14	27
94– 96	17	93– 95	10				188–190	14	25
96– 98	17	95– 97	2				190–192	19	12
98–100	4	97– 99	4				192–194	14	11
100–102	1	99–101	1				194–196	15	3
102–104	2						196–198	16	—
							198–200	9	2
							200–202	6	—
							202–204	4	1
							204–206	4	

mensurations anthropologiques avec la natterie d'instruments de *Martin*. Les résultats sont désignés sur le tableau 5 et sur les tableaux I, II et III.

La comparaison des résultats obtenus avec ceux d'avant démontre un accord parfait. Il est impossible de prouver que le mêlé de sang européen ait eu une importante influence sur les marques anthropologiques mensurables des Groenlandais du sud-ouest.

Zusammenfassung.

Die vorliegende anthropologische Untersuchung wurde im Sommer 1939 an einem Teil der Bevölkerung der Südwestküste von Grönland durchgeführt. Theorien, die über den Ursprung dieser Bevölkerung bestehen, wurden erwähnt, und die besonderen Lebensbedingungen kurz beschrieben.

Table V.

Distribution of the greatest head-width, the cheek bone width, the morphological facial length and the cephalic index.

Greatest head-width			Cheek bone width			Morphological facial length			Cephalic index		
mm	M	F	mm	M	F	mm	M	F	Index	M	F
131–134		1	126–129		2	101–104		1	69–70		1
134–137		1	129–132		7	104–107		3	70–71		—
137–140		10	132–135	4	23	107–110		1	71–72	1	1
140–143	2	17	135–138	3	34	110–113	2	6	72–73	3	4
143–146	12	38	138–141	12	28	113–116	3	19	73–74	—	2
146–149	18	39	141–144	18	23	116–119	5	13	74–75	12	7
149–152	25	17	144–147	34	14	119–122	10	34	75–76	11	11
152–155	29	11	147–150	25	9	122–125	16	32	76–77	8	16
155–158	21	6	150–153	21	1	125–128	25	19	77–78	14	21
158–161	10	2	153–156	7		128–131	25	8	78–79	17	20
161–164	5		156–159	2		131–134	16	3	79–80	22	16
164–167	6		159–162	1		134–137	12	2	80–81	10	10
			162–165	1		137–140	8		81–82	10	15
						140–143	3		82–83	6	8
						143–146	1		83–84	6	5
									84–85	7	3
									85–86	2	—
									86–87	1	1
									87–88		—
									88–89		1

Die untersuchte Bevölkerungsgruppe besteht zum Teil aus unvermischten Eskimos, zum Teil aus solchen, die mehr oder weniger große Beimischungen von europäischem Blut empfangen haben.

Das Gesamtmaterial umschließt 130 männliche und 142 weibliche Individuen. Es wurde eine allgemeine Charakteristik der Erscheinungsform gegeben, beruhend auf anthropologischen Messungen mit *Martin*'s Instrumentarium. Die Ergebnisse finden sich in Tabelle 5 und in Tabellen I, II und III.

Der Vergleich mit Ergebnissen früherer Untersuchungen zeigt gute Übereinstimmung. Es kann nicht bewiesen werden, daß die europäische Beimischung einen wesentlichen Einfluß auf die meßbaren anthropologischen Merkmale der Südwestgrönländer hatte.

BIBLIOGRAPHY

1. *Bertelsen, A.:* The Greenlanders of the Present Day, Greenland, Vol. III, p. 376, Copenhagen-London, 1928. – 2. *Birket-Smith, K.:* Eskimoerne, København 1927. – 3. Id.: The Greenlanders of the Present Day, Greenland, Vol. II, p. 10–56, Copenhagen-London, 1928. – 4. Id.: Anthropological Observations on the Central Eskimos. Report of the Fifth Thule Expedition, Vol. III, No. 2, Copenhagen, 1940. – 5. Id.: Am. Anthropol. *32*, 608, 1930. – 6. *Cummins* and *Fabricius-Hansen:* Am. Journ. of Physic. Anthrop. Vol. 4, No. 3, 1946. – 7. *Fabricius-Hansen, V.:* Journ. of Imm. *38*, 405–411, 1940. – 8. *Fischer-Møller, K.:* The material is deposited in the Institute for Anatomy of Copenhagen. – 9. *Gessain, R.:* Not yet published. The figures are here quoted with the permission of the author. – 10. *Hansen, Søren:* Medd. om Grønland, *7*, 168, 1893. – 11. Id.: Medd. om Grønland, *39*, 1914. – 12. Id.: Nord. Tidsskrift, 1922. – 13. *Jenness, D.:* Report of the Canadian Arctic Expedition. XII, Ottawa 1923 (quoted by K. Birket-Smith). – 14. *Kemp, T.:* Statistiske Metoder i Medicin og Biologi, København 1942. – 15. *Martin, R.:* Lehrbuch der Anthropologie, 2. Aufl., Bd. I, Jena 1928. – 16. *Mathiassen, T.:* Am. Anthropologie *32*, 591, 1930. – 17. Id.: Medd. om Grønland, *92*, 1, 1932–34. – 18. Id.: Medd. om Grønland, *118*, 114, 1936–37. – 19. *Pittard, E.:* Bull. de la soc. neuch. de géograph., XIII, Neuchâtel 1901 (quoted by K. Birket-Smith). – 20. *Poulsen, K.:* Medd. om Grønland, XXVIII, København 1909. – 21. *Shapiro, H. L.:* Anthropological Papers of the American Museum of Natural History, XXXI, New York 1931 (quoted by K. Birket-Smith). – 22. *Seltzer, C. C.:* The Anthropometry of the Western and Cupper Eskimos. Human Biology. Vol. V, Baltimore 1933 (quoted by K. Birket-Smith). – 23. *Steensby, H. P.:* Medd. om Grønland, *34*, 1910. – 24. Id.: Medd. om Grønland, *53*, 47, 1917. – 25. *Stewart, T. D.:* Field Museum of Natural History, Anthropological Series, Vol. XXXI, No. 1, Chicago 1939 (quoted by K. Birket-Smith). – 26. *Virchow, R.:* Zeitschr. f. Ethnologie, XII, 1880 (quoted by K. Birket-Smith).

BLOOD SINKING REACTION FROM A STATISTICAL VIEWPOINT IN NORMAL MEN AND WOMEN

by GUNNAR DAHLBERG

When trying to evaluate more exactly the sinking reaction from a diagnostic point of view it is necessary to know the normal distribution of this reaction. More detailed statistical investigations of this question are, however, not to be found. *Robin Fåhraeus* (1921) published a small normal material for men as well as women and states that: „With a certain degree of probability all sinking values higher than 9 mm per hour for men and 12 mm per hour for non-pregnant women are counted as pathological". *Westergren* (1924) states without basing his opinion on any more detailed analysis of a normal material that the limit of the pathological values is over 7 mm for men and 11 mm for women. He says his opinion is based upon his observation on a material comprising over 300 healthy individuals. *Westergren* does not state further the reason why he differs from Fåhraeus and he expresses himself less carefully. *Lindstedt* (cit. *Sahlgren* 1931) states that for men the values are not pathological until they exceed 10 mm, and that one cannot be certain that they are pathological until they exceed 20 mm.

In the nineteen thirties when systematic medical examinations with regard to the occurrence of tuberculosis were made on all the students newly arrived at the university of Uppsala, sinking reactions were taken regularly. All individuals who showed a high value, or other suspected symptoms, were more thoroughly examined. The values for those in whom no sign of illness could be found (2164), were used as basis of this work. The material was firstly divided into men and women, namely 1770 men and 394 women. That sinking reactions usually give higher values in women than in men is a well-known fact. This is particularly the case during menstruation. Therefore it would be of interest to distinguish between those women who had menstruation at the time of examination, and those who had not; but unfortunately we have no information on this point. In the following, men and women are treated separately.

We have furthermore distinguished between those who showed positive Pirquet reaction, and those who showed a negative one. No difference between these groups was, however, to be found. For men the difference between positive and negative was $+ 0.2 \pm 0.17$, and for women $+ 0.1 \pm 0.64$. (It must be remembered that those with positive Pirquet showing suspected signs of tuberculosis are not included in the material.) We have, therefore, amalgamated the two groups into one in the following.

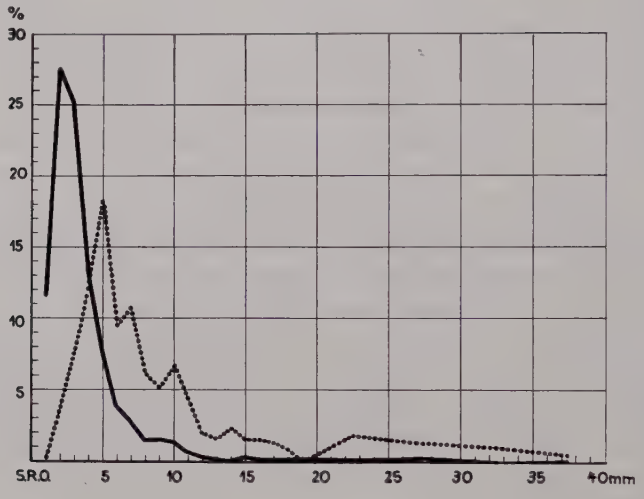


Fig. 1. Distribution of the sinking reaction in normal men and women. Absolute values.

The main purpose of this investigation is to caracterize the normal distribution. This is given for men and women in Table 1 and Figure 1. It appears from these that the distribution shows a considerable skewness and that extreme values are found especially for women. The skewness for men is $- 3.4 \pm 0.03$ and for women $- 1.5 \pm 0.06$. According to *Odenius* (1927) and *Schnell* (1928) a similar distribution is found for conscripted men.

It is difficult to say what the skewness of the distribution depends upon. It is not unusual that biological characteristics, which have a mean close to 0, show a skewness in the distribution. It can

Table 1.

Distribution of the sinking reaction in men and women. Absolute and percentage values.

S. R.	Men		Women	
	Number	%	Number	%
1	206	11.6	1	0.3
2	488	27.6	15	3.8
3	446	25.2	30	7.6
4	236	13.3	48	12.2
5	138	7.8	72	18.3
6	69	3.9	37	9.4
7	49	2.8	42	10.6
8	27	1.5	24	6.1
9	29	1.6	20	5.1
10	24	1.4	26	6.6
11	12	0.7	17	4.3
12	5	0.3	7	1.8
13	4	0.2	6	1.5
14	2	0.1	9	2.3
15	6	0.3	6	1.5
16	4	0.2	6	1.5
17	3	0.2	5	1.3
18	4	0.2	3	0.8
19	3	0.2	—	—
20–24	4	0.2	7	1.8
25–29	6	0.3	5	1.3
30–34	—	—	4	1.0
35–39	2	0.1	2	0.5
40–44	1	0.1	—	—
45–49	1	0.1	1	0.2
50–54	—	—	1	0.2
55–59	—	—	—	—
60–64	—	—	—	—
65–69	—	—	—	—
70–74	1	0.1	—	—
Total	1770	100.0	394	100.0

be stated that the skewness from a formal viewpoint depends upon the fact that negative values cannot exist, and that the nil point, therefore, forms an absolute limit to the variation which becomes compressed, so to speak, from the nil point.

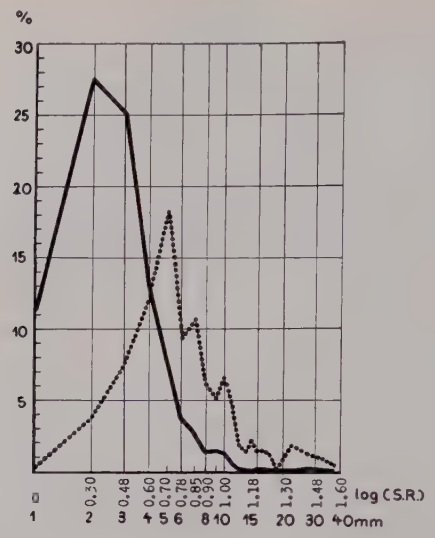


Fig. 2. Distribution of the sinking reaction in normal men and women. Logarithmical values.

If the problem is considered from a physical viewpoint, one may perhaps also suspect the following mechanism. The sedimentation rate is mainly conditioned by the size of the aggregations which are formed by the red corpuscles. If the aggregations are large, the corpuscles will sink rapidly and vice-versa. The rate of sinking can from this viewpoint be said to constitute a measurement of the size of the aggregated red corpuscles.

In order to obtain a concrete picture of the mechanism one may say that when the sedimentation rate increases, the aggregations merge together to a greater degree. If this means that the doubling of the aggregations has an unequal and increasing effect, for example from 4 to 8 and from 8 to 16, then the distribution will become distinctly skew.

I have no reason to go into further detail here as regards the physical mechanism of the sedimentation rate, and this problem could neither be considered fully analysed. It has already been discussed by Fåhraeus to what extent Stokes' law is valid. This law applies to spherical particles. These sink in the beginning with accelerated velocity. Due to the increased friction, the acceleration grows smaller and smaller and eventually an equilibrium is reached

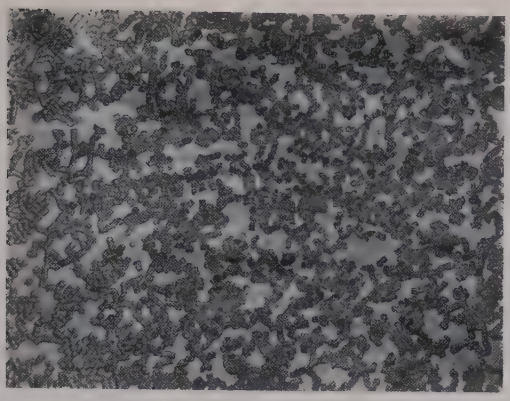


Fig. 3. More or less reticular distribution of the red corpuscles at a micro-sedimentation rate of 3 mm/per hour.

when the acceleration is 0, and when the particles sink with a constant velocity. This equilibrium is proportional to the square of the radius of the sinking particles. Furthermore, this law is only true when assuming that the density of the particles is not too great. It is, therefore, evident that the sedimentation rate cannot be deduced from this law, but, on the other hand, it is also evident that the sedimentation rate must in some way be dependent upon the size of the aggregations. It is possible that those factors which condition

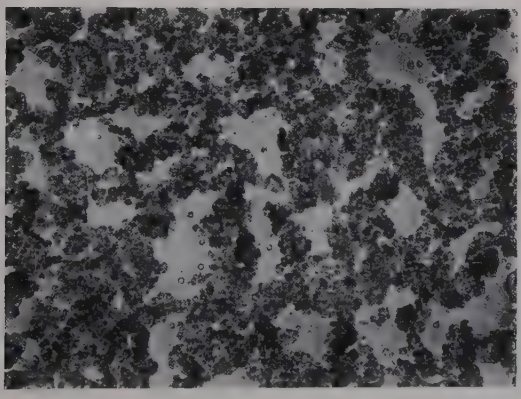


Fig. 4. Appearance of the blood in the preparation shown in fig. 3 after dilution with an equal amount of its own plasma. The micro-sedimentation rate is now 35 mm/per hour.

the size of the aggregations are normally distributed but have an effect which is not normally distributed but according to, for instance, a logarithmical curve. Irrespective of whether this way of thinking is correct or not, it is at any rate of interest to examine what the distribution is if the analysis is based on the logarithms of the obtained values. If this is done the graphic distribution becomes considerably more normal. (See Fig. 2). The absolute values give for men a mean which is 3.8 mm and a σ which is 3.87 mm. If logarithms are employed, a mean = 0.271, i. e. 3.0 mm, and a σ = 0.271, i. e. 1.87 mm, are obtained. As regards women, the absolute values give a mean = 8.1 mm and a σ = 6.33 mm. If logarithms are employed the corresponding values become: mean = 0.824, i. e. 6.7 mm, and σ = 0.262, i. e. 1.83 mm.

In a normal distribution it is to be expected that practically no individual is found outside + 3 σ namely 1 : 370. Outside $\pm$ 2½ σ is found 1:80, and outside $\pm$ 2 σ is found 1 : 22. If the absolute values are used that are obtained from healthy individuals, the distribution, however, as shown does not become normal. On the other hand, if logarithms are employed, the distribution is approximately normal. The skewness which then exists is only — 0.33 $\pm$ 0.03 for men and — 0.21 $\pm$ 0.06 for women, and can therefore be considered so moderate that it is unnecessary to take it into consideration. It can accordingly be maintained that only 0.14 % are found beyond + 3 σ from the mean, and that values above this limit are practically always pathological. So the limit of normal values for men is log 1.293, i. e. 19.6 mm, and for women log 1.610, i. e. 40.7 mm. Those values which are found slightly within this limit may occur in healthy persons but are in the majority of cases expressions of pathological processes. If the values are within + 2½ σ the probability that they occur in healthy individuals is, as previously pointed out, 1 : 80. One is not allowed to invert this rule and maintain that the probability of their belonging to the category sick individuals is 79 : 80. If such a figure is actually found in a patient, one only knows that it is unusual in healthy people, but the individual in question may very well be such an unusual healthy person. In order to illustrate the question we shall give an example.

With respect to the height of normal men in Sweden it can be said that the chance of a man having a height lower than 1.60 cm is 0.093, that is, it occurs in 1 case out of 452. The chance of the same height among normal women is 0.3336, that is, it occurs in 1 case out

of 3. Consequently, the probability of an individual with this height being a woman is 94.5, and a man 5.5 %. In other words, if one only knows the height of the person concerned, the odds are 17 to 1 that the individual is a woman. If in this reasoning one considers the women as representing something pathological, a similar conclusion can be drawn as regards health and sickness. Unfortunately, no materials of sick people have been subjected to such a thorough treatment in regard to sinking reaction that we can make such a comparison from a numerical viewpoint, and it is evident that to do so is very difficult. One has to analyse different pathological materials statistically as regards the sinking reaction. In addition to this one can delimit what is to be called pathological in different ways. It is obvious that a satisfactory statistical analysis of the situation would imply an enormous amount of work. It is, however, valuable to know where the normal ends and the pathological begins, and from this point of view the limits 20 mm and 40 mm can be applied to men respectively to women. Concerning values below these limits one can not draw a definite conclusion from the sinking reaction only, but it is clear that the probability of values near the limit being pathological is relatively great. From a practical viewpoint it might be appropriate to allow for one interval where the sedimentation rate is doubtful, and one interval where with certainty it can be considered as normal. The former interval could be delimited from the mean plus twice the standard deviation to plus 3 times the standard deviation. The uncertain interval then becomes 10–20 mm for men and 22–40 mm for women. These limits should be somewhat higher than those previously reckoned with.

In view of this, it is necessary to discuss in greater detail what is meant by normal from a medical viewpoint. Now and then an à-prioristical conception is used. The normal then is an ideal which need not occur in reality. In other cases an empirical standard is used which is based upon the range of variation and the average of the healthy population. In order to illustrate further the difference between these two standards we shall take an example from another field. As regards caries, a set of teeth can be considered "normal" if it is exempt from caries, and this is so in spite of the fact that there are very few adults who do not suffer from caries. It can, however, also be stated that a person has caries to a normal degree for his age. It is clear that the word "normal" has different meanings in these two cases.

One can reason both ways concerning the sinking reaction. On the one hand it can be maintained that the normal is a person who has not been exposed to infections; on the other hand, that a person is normal when he does not show, or during the near future is not going to show, signs of a disease. In the latter case, those persons for whom a physician would be willing to issue a health certificate are considered as normal. It is in this sense that we use the word "normal" in this work. The reason for this is that it is practically impossible to pick out those who have previously suffered from an infection but who at present do not have symptoms, or suffer from an infection which gives no symptoms. It is evident than when one uses the sinking reaction in order to distinguish between sick and healthy peopl-, it is not justifiable to draw too narrow a limit.

Originally *Fåhraeus* emphasized that the sinking reaction was increased in pregnant women, and thought that it should be possible to use it as an aid for diagnosing pregnancy. Later on, more reliable reactions of pregnancy have been found, which is why the sinking reaction has not been so greatly applied for diagnosing pregnancy as one would have expected.

The limit between pregnant and non-pregnant women is naturally more sharp than between sick and healthy people. One must, nevertheless, take into consideration that in a normal material of women, pregnant women may be found who are not as yet aware of their own condition, or who recently have had a miscarriage. In our material, however, such individuals, if any, should be very few.

If instead of a normal material made up of people who seem to be healthy for the moment, one uses a more strict delimitation, it is necessary to eliminate those who have been ill or are going to be ill in the near future. This can hardly be done. It is impossible to say how long an interval must be reckoned with before illnesses which give increased sinking reaction begin to show symptoms. If only one is patient, of course we all become ill and die. Especially difficult is therefore to evaluate a subsequent illness, as one never can be absolutely certain that it is connected with a previously increased sinking reaction. Furthermore, it involves a great amount of work to produce such an ideal material and it should have no practical significance because the sinking reaction is not used in order to find cases quite without illness, but to distinguish in practice sick persons with different kinds of symptoms from healthy ones. Whatever standard is

applied one must take into consideration that some few extreme values occur. In biology sharp limits are seldom found.

Finally, it must be pointed out that the normal material collected by *Fåhraeus* shows good agreement with ours, and that he has used the same kind of standard as we. Thus, he finds that 4.8 % of the men show values exceeding 9, and 8.1 % of the women show values exceeding 12. For the rest also, *Fåhraeus*' material shows, in spite of its smallness, good agreement with ours. The mean is 3.3, and σ is 4.15. If one uses logarithms, the corresponding values are 2.6 and 1.98 for men. For women, the mean is 7.6 and σ 4.15. When using logarithms, the corresponding values are 6.5 and 1.64 respectively. It should be pointed out that the higher values for women partly are connected with their having a lower number of red corpuscles than men. A decreased number of red corpuscles increases the sinking reaction, and therefore it is increased in pronounced anemia. See figs. 1 and 2.

In any case it must be emphasized that the above-mentioned limits do not signify that individuals with these values are healthy, but only that they may be healthy, though not very often. Within the limits stated by us, 10 mm for men and 21 mm for women, the probability that an individual is healthy is relatively great. In the interval between 11 and 20 mm for men and between 22 and 40 mm for women, this probability is very small, but such values may occur in individuals who do not show symptoms of illness or whose symptoms, if any, are not connected with the value of the sinking reaction.

Finally, it should be emphasized that all this applies to single determinations. If values near the limits are obtained at repeated analyses during a long time, of course there is reason for suspecting a latent infection. Further, the values given only apply to young persons. In old persons, the values of the sinking reaction are considerably higher as far as one can judge from an analysis of a small material of old individuals which will be published later.

Summary

Sedimentation reaction was performed on 1.770 healthy male and 394 female students. The figures obtained show a very skew distribution. It is shown that when using logarithms for the figures the distribution is nearly normal. Therefore, the standard deviation obtained from the logarithms can be used when deciding the range of variation in healthy persons.

Résumé.

La vitesse de sédimentation du sang a été examinée chez 1770 étudiants en bonne santé du sexe masculin et 394 du sexe féminin. Les chiffres obtenus indiquent une distribution asymétrique. Si l'on se sert des logarithmes pour l'interprétation des chiffres obtenus, leur distribution est à peu près normale. Ainsi la dispersion étudiée à l'aide des logarithmes peut être utilisée lorsque l'on doit déterminer l'ampleur des variations chez les personnes en bonne santé.

Zusammenfassung.

Blutsenkungsreaktionen wurden an 1770 gesunden Studenten und 394 Studentinnen geprüft. Die erhaltenen Zahlen weisen eine sehr schiefe Verteilung auf. Es wurde gezeigt, daß bei Anwendung von Logarithmen die Verteilung dieser Zahlen beinahe normal wird. Deswegen kann die auf logarithmischem Wege erhaltene Streuung angewandt werden, wenn man die Variationsbreite des gesunden Menschen zu entscheiden hat.

LITERATURE CITED.

Fåhraeus, Robin: The suspension stability of the blood. Stockholm 1921. – *Odenius, R.:* Tidskr. f. militär hälsovard, 1927: 52, 203. – *Sahlgren, Ernst:* Acta Med. Scand. 1931: 77. – *Schnell, R.:* Hygiea, 1928: 90, 658. – *Westergren, Alfr.:* Ergebn. d. inn. Med. u. Kinderheilk. 1924: 26.

THE FREQUENCY OF CASES OF DISEASE

by GUNNAR DAHLBERG

Introduction.

Great difficulties are encountered in making up reliable statistics of disease. Often the physician does not have a clear idea of the elementary methods to be used. A statistician possessing the necessary statistical knowledge is often out of touch with the practical difficulties and overestimates the data at his disposal. Actually the conception "disease" is not clearly defined. This makes a difference especially as regards mild cases of disease on the borderline between illness and health, and also with respect to diseases in old people. For it is difficult to decide what is "normal" for old persons and what is due to disease. It should lastly be kept in mind that the cases of disease we accord a certain diagnosis are not quite alike; they are more or less heterogeneous and when we assume that a certain diagnosis is correct this implies only that we group the cases together with other similar cases. Formerly this sorting was made on different principles. Therefore diagnoses of bygone days cannot be used. In future our diagnostic system will certainly be subjected to many changes. This implies that the classification we are using today will become useless in future. Therefore the statistics of disease now being made can be expected to become obsolete more or less soon, particularly as the social pattern constantly changes and accordingly the frequency and character of diseases. Nevertheless it is of great interest to society and also to physicians to get as reliable data as possible on the frequency of disease.

The frequency of becoming ill.

Medical textbooks as a rule try to tell how commonly a given disease occurs. Sometimes there is a small paragraph entitled "the frequency of the disease". Often, however, the data given under this heading are very unreliable and have sometimes very little to do with the frequency of the disease. Actually, on the basis of a single figure it is almost impossible to say how common a disease

is, i.e. what the risk is of getting the disease, which in fact is what we wish to find out. Naturally the risk of getting a disease usually is very different in different ages and sometimes it also is different for men and women. As a rule adults do not get childrens' diseases like mumps. Men do not get obstetric disorders but they oftener suffer the results of other accidents. The number of persons in a population who annually get ill is dependent, then, both on age and sexual distribution. If, for example, we compare the percentage of diseased persons who are women in a metropolis like Stockholm and in a rural district the figures will be very different because women are in majority in Stockholm but in minority on the land. The difference is by no means negligible. If we caricature the chosen example and set out from a population consisting solely of women none of the diseased in the population can, of course, be a man. Thus, the sexual proportion obtained among the diseased obviously depends on the population from which the material is taken.

Often the sexual proportion is given of hospitalized diseased cases. This proportion, however, is greatly affected by the number of beds available for the two sexes. However, a moderate deviation in the sexual proportion can be compensated by overcrowding and by keeping the patients in the hospital for shorter times. If the hospital has an equal number of places for men and women the proportion among the patients will be influenced thereby. When hospitals are planned it is necessary to set out from more or less vague ideas of the need for beds for the different sexes. In general it is probably assumed that the requirements are just about equal, but this is by no means necessarily the case. When the situation later is to be studied the figures will, however, be biased by the number of beds made available and under such circumstances it is difficult to get figures which correctly picture the situation.

The age distribution of the population plays an important role for the frequency of a disease if past times are to be compared with the present. For example, the increased incidence of cancer must in any case largely be due to the fact that in current times a comparatively large number of persons survive to advanced ages when the risk for cancer begins to become more tangible. (As a matter of fact there is reason to assume that the risks for the different age groups are somewhat less than formerly.) Obviously, furthermore, if populations with a large number of children are compared with populations with a low fertility a considerable difference in mortality will be ob-

tained although the risks of death need not be different for the various age groups. As we know infants have a fairly high mortality. In order to avoid that this age group will make the populations less comparable it is often usual to give the mortality with children under one year excluded. If several age groups are to be compared this measure is, of course, unnecessary but then the figures will instead be difficult to interpret.

These theoretical sources of error can be eliminated by giving the risks for men and women separately and by adding the risks for the various ages and giving the cumulative or total risk up to a given age. As a matter of fact, however, the discussed sources of error are not inordinately large and if an approximate idea is all that is required they may be disregarded.

The by far more important source of error is, however, of practical nature. The frequency of disease obtained is naturally dependent on how the limits are drawn and particularly on whether the mild cases are included. In ideal statistics it should be required that each case satisfied certain criteria; exhibited certain symptoms, etc. However, such an investigation would be very difficult to carry out: the cases must be considered not only according to the condition they are in when they become ill, perhaps the first time they visit a doctor, but with regard to the symptoms they exhibit during the entire course of the disease. In so doing it may be necessary to distinguish between cases of varying degree of severity and make use of several definitions (cf. e. g. *Jönsson* 1938). As a matter of fact in practice one probably has to remain content with a mixture of not quite safe diagnoses of cases which have been examined with varying thouroughness at different periods during the course of the disease. The difficulties are especially great in dealing with cases of chronic diseases. In these it is hard to fix a definite time for the onset of the disease. If we take a disease like diabetes as an example the time when the morbid condition was discovered can certainly be fixed but it is often difficult to tell how long the patient had been ill previously with slight symptoms that did not force him to a doctor. In such cases one possibility would be to give the total number of cases in a population who visit the doctor for the first time in, say, a given year, the period of disease which had elapsed before the visit to the doctor thereby being disregarded. All the cases who do not go to the doctor, i. e. the mild cases who soon get well, will in any case be lost. In this respect conditions are highly vari-

able in different populations, partly because of the varying availability of doctors. This implies that the figures for rural districts tend to be lower even if the number of cases of a disease should be the same. This is, of course, also true if the frequency of hospitalized cases is given. The rural population is often more afraid of hospitals than the urban population and in any case a period of hospitalization implies a greater break for them because they become more separated from relatives and cannot receive visitors so often, etc.

Besides, it should be pointed out that the frequency of hospitalized cases naturally depends on the supply of hospital places. For one and the same number of hospital beds the number of cases may, of course, vary because of crowding or the opposite, but the limits between which the number of cases can vary are, however, more or less determined by the number of hospital beds. In a region where this number is very large some slight cases also will, of course, be treated in hospitals. If despite this the hospital is not filled up the patients will surely be kept longer; no hospital doctor likes to have his establishment fairly empty. In another region where the facilities for hospitalization are not so abundant the patients will certainly be cared for intramurally as short a time as possible; the treatment will have to be completed in the home in order to make beds available for diseased persons who are more in need of care. If the hospitals can take a very small number of patients only, quite a large number of patients will whatever happens have to be treated in their homes although, had the number of hospital places been greater they would have been hospitalized. In such a case the hospitalized patients will in other words include only very sick persons.

Mortality.

It is naturally of especial interest to know the number of cases who have died in a certain disease. If this figure is known we have some idea of how dangerous the disease is. At this point, however, it must be remembered that the number of deaths is proportional to the resistance of the patients. Therefore a higher mortality is to be expected in a population which is in an inferior physical condition, e. g. after a war. We can chiefly expect a high mortality in old persons whose resistance is not very great and in infants to whom the same applies. Consequently the mortality in a certain disease must not be given in relation to the number of cases of that disease without paying

regard to the age. Certainly it also is suitable to pay attention to sex although the evidence is not so certain that the mortality calculated on the basis of the number of cases of the disease is different for the two sexes. However, precisely because we have little reliable knowledge on this point it would be interesting to obtain such figures.

Naturally, the death rate may also be given in proportion to the population and this is indeed the method most commonly employed in vital statistics. This method of computation has, of course, been adopted because it was impossible to obtain reliable data on the cases of disease so that the mortality could be related to the respective diseases.

I wish to draw attention to only one more thing. When an increase, if any, of the mortality is given it is usual to give it as a percentage of the previous mortality. This is equivalent to assuming that if the mortality doubles for one age group it will also be doubled for the other age groups and for both sexes. This may be the case but is, especially if the increase in mortality is large, by no means certain. In order to make my meaning clear I shall give an example. *Maltzberg* and later *Alström*, from whom the following figures are taken, have shown that institutionalized mental cases have a higher mortality. The mortality of mental patients in hospitals in Stockholm is 3.6 per cent in the age group 20–25 years and the corresponding figure for the entire population of Stockholm is 0.40 per cent. Thus, the mortality of the mental cases is 9 times as large as that of the normal population. Mental cases in the age group 60–65 years have a mortality of 7.5 per cent; the corresponding figure for the population of Stockholm is 2.5 per cent. Accordingly the mortality of old mental cases is only 3 times as large as that of the normal population. If, on the other hand, we set out from the absolute differences the increase in the young patients amounts to 3.2 per cent and in the old to 5 per cent. Therefore, judging by the absolute differences, the old will have a much more increased mortality than the young. The correct way of looking at these things is, of course, dependent on other aspects of the situation. Supposing now that mental cases intrinsically have a normal mortality and that their excessive mortality was due to an airraid which by chance had been about equally fatal to all age groups then the absolute difference would, of course, be the correct denotation for the excess mortality. If, on the contrary, the increased mortality is due to a more frequent incidence of fatal tuberculosis in the mental cases the former way of looking at things may perhaps be

more to the point. It is in any case theoretically more satisfactory in some respects. In order to still more clarify my meaning I shall take an example from another field. Suppose that in a given election 80 per cent of the men vote but only 60 per cent of the women. In another election the number of voters may be greater because the weather happened to be especially nice. It appeared that 90 per cent of the men voted. How high should the percentage be for the women if they are as susceptible to the nice weather as the men? It is unreasonable to presume that they also increase by 10 per cent, i. e. to 70 per cent. For there are more women to be stimulated by the weather then there are men. If we assume that half of those who did not vote the first time voted the second time the figure for the women would be 80 per cent, e. g. the increase would be far larger than for the men despite the assumption that both sexes were equally susceptible to the weather. It must analogously be determined if a proportional increase of the mortality would be reasonable in the situation at hand or if the absolute differences are more properly used.

Also in an investigation of mortality the primary difficulty is not a methodical but a practical one. It is often difficult to obtain reliable death diagnoses. In this respect the situation is worse in rural districts than in cities in this country because almost without exception a doctor's death certificate is available in the latter case at least in Sweden. However, even in such a case the cause of death may be difficult to ascertain. We have to distinguish between primary causes of death and contributory causes of death. Of course, it often is easy to decide which is which but in quite a number of cases one is confronted by unsurmountable difficulties. For example, when we are dealing with deaths in diabetes the fact of the matter is that diabetes often is given as the cause of death although the patient died in another disorder, e. g. pneumonia. Diabetics are especially susceptible to pneumonia and in the individual case it often is impossible to decide whether the patient died of his diabetes or because he succumbed to pneumonia. When it is a matter of a large number of cases it may be assumed that diabetics should be struck by pneumonia with a normal frequency for their age and only the excess mortality above this frequency should be due to diabetes. If doctors consistently would give diabetes as the fatal reason for persons having this disorder when they died, it might be possible to correct for it. Because the situation is so unclear it may, however, be feared that doctors adopt very different methods.

It is especially deplorable that official statistics give the various causes of death due to arteriosclerosis under different headings. Nor is it possible by adding these groups to find all the cases due to arteriosclerosis. The methods of combining for example the deaths due to heart failure without sorting out those basically due to arteriosclerosis makes the group far too heterogeneous to be of any use.

Less common methods of computing the frequency of disease.

Often the age and sexual distributions are given in statistics of disease. In itself, however, such a grouping lacks general interest; it might possibly be of importance to general practitioners since from it they may get an idea of the age and sex of their expected patients. If, however, one dare consider the material a correct sampling, a representative selection of the sick in the population, it may be used to get relative figures for the frequency of the disease at various ages of the two sexes. If, furthermore, it is possible to obtain an absolute figure for a certain age group of the population, for example taken from conscripts, this fixed point may be used as a basis for computation of absolute risks from the relative risks of becoming ill and it is thus possible to arrive at the goal by means of a devious route. The method has been employed in a paper by *Dahlberg* and *Stenberg* (1931) with regard to mental disease.

Another more dubious method of estimating the frequency of disease is to give the number who have had the disease in a group of hospital cases. The figure thus obtained cannot be immediately related to the population. If one states that between 2 and 3 per cent of those who have consulted a hospital for some disorder of the eyes are cross-eyed (*Ploman* 1936), the information may, as mentioned previously, possibly be of interest to the physician who receives the patients. He can reckon that about every 50th patient needs to be treated for strabismus but he can get little else out of the figure. The figure obtained would be correct, if you could assume that cases of strabismus were discovered at random among the patients consulting a hospital. As we now know that patients consult the hospital just because of strabismus, the figure must be too high in comparison with the real frequency in the population. If a patient suffers from strabismus or not cannot as a rule be determined at birth. The symptoms appear as the child grows up. If it is known, then, how many annually turn to a hospital for the first time for strabismus, this

number may be related to the number of individuals in the population who survive at the mean age of cross-eyed people. The figure for the frequency thus obtained is fairly correct provided it can be assumed that all cross-eyed children in a district apply for treatment at the same hospital. When hospital cases are used to compute frequency figures which may be related to the population two things are of importance:

1. That cases who do not belong in the district studied must be rejected.

2. That only an insignificant number of patients from the district applies at another hospital.

The duration of the disease.

In a great number of diseases it is not difficult to determine the duration of the disease. In others, on the contrary, it is impossible to tell exactly when the disease commenced. This is especially true of chronic diseases. In such cases, one may attempt to fix the earliest and the latest moment when the patient first could have contracted the illness. This method yields limit values that may be used in approximate computations. It is easier to give the duration of hospital treatment or the period when the patient was bedridden. However, here no particular technical problems are encountered and the sources of error are obvious so there hardly is any cause to linger on the subject. The only thing I should like to point out is the advisability of distinguishing between the duration of treatment for cases who recover and for fatal cases. It is unsuitable to combine these two things.

The prevalence of the disease.

The number of cases of a given disease in a population naturally depends partly on the magnitude of the risk of getting the disease and its mortality, partly on the persistence of the disease both for fatal cases and for those who recover. Chronic diseases with low mortality and great persistence become fairly prevalent. This is so, for example, as regards psychical disorders. Comparatively common conditions which rapidly are fatal or result in recovery will naturally have a comparatively small prevalence. Cancer is a good example of this. The essential thing, therefore, is that the risk of contracting the disease should not fallaciously be deduced from its prevalence.

Summary.

Various methods of obtaining an idea of the frequency of different diseases are discussed, especially in regard to the errors which may be expected in this connection. The most important source of error seems to be that the disease in question may be delimited in different ways.

Résumé.

Discussion de diverses méthodes permettant de se faire une idée sur la fréquence des différentes maladies, particulièrement au point de vue des erreurs possibles. La cause d'erreur la plus importante semble résider dans le fait que l'affection considérée peut être limitée de différentes manières.

Zusammenfassung.

Es werden verschiedene Methoden besprochen um eine Auffassung über die Frequenz verschiedener Krankheiten zu bekommen, unter besonderer Berücksichtigung der Fehler, die man in diesem Zusammenhang erwarten kann. Die wichtigste Fehlerquelle scheint zu sein, daß die in Frage stehende Krankheit auf verschiedene Weise begrenzt sein kann.

LITERATURE CITED.

Dahlberg, G. and *S. Stenberg:* Zeitschr. f. die gesamte Neurologie und Psychiatrie, Bd. 133, 1931. – *Jönsson, B.:* Zur Epidemiologie der Kinderlähmung. Stockholm 1938. – *Ploman, K. G.:* in Nordisk lärobok i oftalmiatrik. Stockholm 1936.

WHAT DOES NORMAL MEAN?

Analysis of a conception

by GUNNAR DAHLBERG

When we use the word "normal" in everyday speach no serious misunderstandings arise although the meaning of the word is rather vague. In the exact natural sciences, for instance, in chemistry, physics, astronomy and mathematics the word is not so widely used. And when it is used, it has a special meaning which is different from the usual one, for example when in chemistry one refers to a normal solution or in geometry to the "normal" as a synonym of "at right angles". On the other hand, the word is comparatively much used in the sciences which refer to human life, in spite of the fact that no clear definition is given of its denotation. In economics one speaks of "normal times" without being able to explain precisely what the expression actually means. Cautiously one therefore tends to refer to "more normal times" even though here again a definition of what "normal" means is still actually required. In philology one speaks of normal pronounciation and yet is unable to give an exact definition of this term. Generally one refers in this connection to the language of educated people. But such a definition is not exact since even their pronounciation varies within certain limits. Finally, in medicine the word "normal" is often given the meaning of healthy, but also several others. Before discussing this usage, I will, however, consider what the statistician means by normal. For only here is there a clear definition, which at the same time is not too different from what is meant by normal in everyday speach.

The conception of normal in statistics.

In statistics one speaks of a normal distribution or of a distribution in accordance with a normal curve when the object of investigation varies because it is influenced by several factors which occur in combinations at random. The classical example is the distribution which results when one throws dice or coins. The way in which the dice or the coins fall is determined by a mass of different factors as, for instance, initial velocity, air friction, friction against the surface etc. One can either compute on the basis of mathematical probabilities what distribution is to be expected, or one can try empirically to see what actually happens. Both procedures agree very well.

The resulting curve has the shape of a bell; in other words, for the most part one obtains results which lie in the middle of the curve, and the extreme deviations are rare. In the game of heads and tails the resulting distribution falls in classes and follows the coefficient of the binomial theorem.

If we suppose that an infinite number of throws are performed, the various classes coalesce into a continuous curve, precisely as a circle can be supposed to result from a regular polygon with an infinite number of sides. In this way one reaches the normal curve from the so-called Gauss' distribution. Theoretically, the curve extends on both sides from the middle to the infinite.

In statistics everything contained within the area of this curve is normal. Actually, one assumes, however, that the area of the curve only extends from the middle to three times σ on either side. Consequently, this is called the normal range of variation.

The conception of normal in medicine.

In medicine the term normal has several different meanings.

1. In the first place, an *a priori* conception of the normal is sometimes used. For instance, in talking of a normal tooth one means for the most part a tooth which is entirely healthy. In a sense the normal is an ideal, more or less in Plato's meaning. It need not occur in reality. Particularly in fields in which the possibilities of empirical research are not too good, for instance in psychology, such an ideal conception of normal is in use. The *a priori* "normal" person in the psychological sense is a person who can hardly exist. It is a person who is always well balanced, is neither too optimistic nor too pessimistic, is not vindicative but, on the other hand also not too forgiving. It is a question whether these various traits can be found in one person. In any case, an empirical conception of normal, such as one needs first of all in psychiatry cannot be clearly defined because the traits in question cannot be measured. Apart from other reasons the psychiatrists have different views as to the characteristics of a normal person because they must use an *a priori* conception of normal. Probably they therefore admit a different range of deviation before calling a person abnormal. This is one of the reasons why dissent oftens occurs in deciding whether or not a person shows psychological disturbances.

In other branches of medicine also, a conception of normal is used which is to a degree *a priori* – although hardly to the same extent as in psychiatry and psychology. Apart from this conception,

in medicine the word is used in two different meanings, namely, either in the meaning of healthy as opposed to ill, or in the meaning of common as opposed to rare. In both cases the conception must, of course, be founded upon factual observations concerning the characteristics of "healthy" or "common". In other words, the conception of normal is here based on empirical evidence.

2. The contrast between normal and abnormal is in actual fact a contrast with a statistical meaning. The normal is the *usual*, the abnormal is what deviates from the usual. This definition is obviously rather vague and must therefore be discussed. One cannot give a definite answer to the question of how unusual a trait must be if it is to be called abnormal. In order to obtain an exact definition one can perhaps reason as follows:

Average people are subject to the influence of a whole mass of hereditary and environmental factors. The traits which can originate under the influence of these factors may be regarded as normal. Those traits which are determined by other factors, factors which do not influence normal people are sometimes counted as abnormal. In order to clarify our meaning, we shall give a concrete example.

The body length of ordinary people depends partly upon a number of hereditary factors, partly upon a number of environmental conditions. If a person is subjected to an unfavourable combination of hereditary and environmental factors, he either remains particularly short or grows to unusual height. (It is perhaps not necessary to call the combination unfavourable since the body length as such is a fairly indifferent trait.) If, because of such a combination, a person grows to a body length which is less usual, he will nevertheless be regarded as normal. On the other hand, a person may for other reasons attain a height which lies outside the range which can be determined by normal factors. For instance, he can be attacked by an illness which more or less distorts the vertebrae, and as a consequence he remains so short that his body length falls outside the range of the normal. Further he may happen to have a special hereditary factor which makes for dwarf size. The essential is that the person is affected by abnormal factors and therefore eventually deviates from normal people. At the same time, there is no good reason for calling a person abnormal who is short but falls within the range of variation conditioned by usual factors. If one begins to do that kind of thing the task of justifying the assumed limit becomes very hard indeed. In medicine one does not usually apply the points of view given here; rather one calls a person abnormal if he deviates

from what is common without clearly justifying the limits which have been assumed, often even without mentioning any particular limits. In a practical sense such a usage involves no major difficulties. Only in the course of special scientific investigations do difficulties actually appear. For the most part, this is the case with investigations of a statistical character which have the purpose of analyzing the conditions prevailing in a population.

In the preceding discussion I wanted only to point at a possibility of giving clearer definition. Naturally the definition which has been outlined has nothing to do with illness and health. A person of short stature can obviously not be regarded as ill merely because of his small size. On the other hand it is true that persons who deviate from the normal often are ill. At any rate it is most commonly for this reason that their deviations arouse our attention and interest. Obviously, there is nothing to prevent a person's being ill although he falls within the range of the normal, even though this does not often happen. For example, if one investigates the normal range of variation with regard to the number of red blood corpuscles one finds that there are some persons who have difficulties owing to their comparatively low number of such corpuscles. Yet, others with the same amount of red blood corpuscles may be free from difficulties and thus healthy. Nevertheless one often uses the conceptions normal and abnormal as equivalent to the conceptions healthy and ill. In the latter case an entirely different contrast of conception is, of course, involved.

3. When using the term normal in the meaning of *healthy*, one needs a definition of illness. It is, however, not easy to give such a definition. All people know what is meant by illness. But in scientific investigations a clear delimitation is required. And in the attempt to find a delimitation one meets with obstacles. Particularly when it is a question of mental illness, dissentions sometimes arise as to whether or not a certain person or group of persons are to be regarded as ill. One can perhaps say that a diseased person is a person who has unintentionally a lowered level of achievement. But we regard also a person with a normal level of achievement as ill if we know that he will have a lowered level of achievement in the near future. For instance, if one discovers that a person has cancer of the stomach but has not yet suffered from it, he will be regarded as ill. To be sure, we must all count on the probability of finding our level of achievements lowered at least some time before we die. With regard to this risk we might all be regarded as ill. The reason why we regard the cancer

patient as ill in our example is simply that we happen to have more exact knowledge of the time in which his level of achievement will be lowered. In actual fact it may happen that the physician who makes the diagnosis and who regards himself as healthy will find his own level of achievement lowered earlier than the cancer patient. This phase of the conception of illness is in other words quite unclear. On the other hand if we limit the conception of illness to persons whose level of achievement is already lowered the difficulty arises that we can not explain what is meant by a normal level of achievement. The level of achievements varies from one person to another, and it may happen that it is higher with a diseased person than with another whom we regard as healthy.

The conception of illness may under these circumstances be referred to the level of achievement which characterizes the person in question as a rule, and one can consequently regard a person as ill when he has a lower level of achievement than he had before.

The level of achievement is, however, connected with the age. It is lower in children and old people than it is in persons of middle age. Particularly when it is a question of old people one cannot be satisfied with the statement that a person is ill if his level of achievement is lower than usual. What is usual for an old person may precisely be that he is ill. The conditions of illness which are related to high age must be judged in relation to other people in the same age group. Thus one says of a person that he still has his teeth to the extent which is normal for his age. A person who deviates from the level of achievement which is normal for his age must occasionally be regarded as ill. For a person to be regarded as ill it is, however, necessary that the lower level of achievement be connected with certain processes which occur in his body. It is especially difficult to distinguish such processes as belong to normal ageing from processes which cause illnesses connected with age. If the problem is to be fully discussed, one has, in other words, to consider various kinds of invalidism. What distinguishes invalidism from illness is precisely the fact that in the case of invalidism there is no developing process. Invalidism may be a consequence of illness. The process of the illness may have come to an end but may have left defects behind. Actually there is no sharp boundary between a chronical disease and invalidism. As a result, it is an extremely hard task to give a theoretical definition of what is meant by normal in the sense of healthy and by abnormal in the sense of ill. It is therefore not astonishing that, in actual practice, differences of opinion are by no means rare. At present it would

be impossible to achieve an exact delimitation of the conception normal in the meaning healthy. In scientific investigations a special definition must therefore be given which serves to delimit the illness in question. A general exact definition of the various conditions of illnesses with which one works in medicine cannot be given and therefore also no generally valid and exact definition of what one means with healthy.

The conception of normal in art.

About art the word normal is often used in a degrading sense. In the attempts to be artistic one tries to be original, that is to deviate from the usual. Generally it is so that things that we are used to seem boring to us. But that which deviates too much from what we are used to is shocking to us. In art one is successful if one is moderately original, compared to what is prevalent at the moment. Too much originality arouses a more or less strong aversion until the usual has changed and it no longer appears to be very original. Then the expert will tell us how very daring the thing was at the time it was produced. The conditions are, of course, different in different kinds of art.

In music one usually only distinguishes between good and bad music. If some music is considered abnormal one seldom means to imply that it is unhealthy. One only means to say that it deviates from the usual too much, for instance, that it hurts our sense of harmony (*Schönberg*). One often asserts that it is not genuine art and that the composer is only trying to produce a sensation or something like that. That music is so seldom considered to be unhealthy is, of course, due to the fact that there is so little similarity between abnormal music and the symptoms of illness. Musical symptoms are not common in psychical diseases. Therefore the points of view mentioned above are applied more exceptionally. However, it has happened that a psychiatrist whose wife was a singer and was unfavourably criticized, stated as his opinion that the reviewer suffered from a disturbance in his sense of harmony and therefore could not judge good music.

In literature it is much more common that a certain work is considered unhealthy. This means usually that it is considered below the standard as a work of art. However, the fact that a novel originates from unhealthy imaginations does not necessarily signify that it is below the standard from an artistic point of view. For example the "Ulysses" by *James Joyce* evidently shows traces of schizophrenic disposition which found a more incomprehensible expression in the

"Finnegan's Wake". In spite of this it is highly appreciated as a work of art. It is especially when literature elaborately and openly deals with sexuality that it is considered abnormal. This is so only when one has no reason to assume that the author is merely trying to take advantage of people's interest in sexuality, but means it honestly. On the other hand people sometimes try to defend a certain tendency towards sexuality by saying that the author is a Renaissance-type, that he is sound and sensual etc. In any case one might say that the normal is not the only aim in literature and that on the other hand the abnormal in the sense of not normal and not healthy is nothing derogatory in itself.

One criticizes persons who are not adherents of absolute values when in the field of art they have any values at all. If one has no absolute values, valuing ought to be impossible. When it is a question of valuing one can refer to what is common for the majority of people. But when it is a question of value judgments concerning art this way out is hardly acceptable. The minority will not yield to the majority. The majority of a people likes, for instance, accordian music and finds that symphonies of *Beethoven* and *Mozart* are utterly boring. With full right they say that those symphonies do not give them any feelings of beauty. Those who enjoy symphonic music can, however, not be persuaded to accept accordian music as high art. On the other hand, one cannot refer to the judgment of minority unless one has precise criteria as to how that minority is to be selected. Before going any further we will, however, discuss art with reference to the conception of normal.

The line of demarcation between normal and abnormal is of greater importance in the art of painting.

Those who belong to my generation have had abundant opportunity to see that what for several generations was condemned as abnormal and unhealthy in art later has been regarded as great and high art. This reversal in the general opinion which has taken place has first of all to do with the experts, but it is quite obvious also in a broader public. Those who from the first took sides with the abnormal art believe with a feeling of triumph that they have won their point.

When confronted with a certain work of art, the experts may be in doubt. They may perhaps say that it is still too early to judge its value, and thus they point towards a future opinion. In other cases they are sure of their judgment and prophesy that they will win their point. In other words, they sometimes appeal to an opinion of the

future, however, not an opinion of the masses but to that of the experts. Commonly, one also points out that the opinion of the large public follows that of the experts, although with a lag.

When abnormal art is to be distinguished from normal art one thus refers to the opinion of persons who have had a technical training but are so young that they are not yet prejudiced. In case of doubt one cannot always rely on the judgment of those who are now regarded as experts, because these may have become fixed in a certain system of valuations. It may be that one can obtain a certain objectivity in the field of art by saying that normal art is what most people would regard as beautiful if they were trained, while abnormal art is what only a few would like after being trained. In order to clarify what I mean I will give an example.

Most of *Picasso*'s art has in former times aroused enormous opposition. At present *Picasso* is in many places counted among the worlds' greatest living artists. Nevertheless even for persons who have a good education in the field of modern art some of *Picasso*'s work especially the later one is repelling and far from beautiful. One argues in certain circles that *Picasso* is mentally ill, that several of his works are symptoms of a form of schizophrenia, in other words of a pathological process. Even if this were true, the work could still belong to the sphere of art. That *Picasso* thinks so himself, ought to be beyond any doubt. The only thing one can say in this situation is that, if persons who have training and who are not fixed in a certain opinion, should later regard these works as beautiful, the paintings will also be recognized as works of art. In case this does not happen, they will in the future be regarded merely as results of an abnormal condition in *Picasso*.

Above we have discussed valuations in the field of art for the reason that if one wishes to distinguish between unhealthy and normal art such valuations play the principal role. When pointing out that certain works are conditioned by pathological processes in the artist the argument is in itself, of course, rather irrelevant. First of all, in order to maintain that it is a question of unhealthy art one would have to prove that the artist has been ill or mentally abnormal. Even if this can be done, the works which he has produced during his illness may still be all right as for example the paintings which *van Gogh* produced while he was in the insane asylum at Arles. One can say that the pathological process had not yet influenced his power of painting. One can assume that, if the pathological process had gone further, it would have done so, as was the case with the Swedish

painter *Ernst Josephson*. In any case it is, of course, not possible to draw a sharp line between unhealthy and normal art. Only in extreme cases can we with any assurance make statements in this respect.

In applying the form of reasoning here outlined, which seems to follow the general usage, one does not, of course, obtain an exact definition, and, what is worse, it remains a matter of historical periods what goes as normal. It cannot be decided once for all.

In other words, the conception of normal receives a different interpretation in different fields. The only common ground is that it be based on something which is usual, even if the range from which one selects the usual is delimited in widely varying ways. No exact and generally valid definition of the normal seems to be attainable. The main cause of this seems to be that the conception of normal includes some sort of valuation which of course is more or less variable.

Summary.

In everyday speech we use the word normal meaning what is usual and to us seems all right. In different sciences the word has different meanings. In this paper the conception is especially discussed from a medical point of view but also from the point of view of art (literature, music and painting). It is shown that in most connections the normal is the usual but that also a judgment of value is included in the word.

Résumé.

Dans le langage quotidien, le mot *normal* représente ce qui est usuel et ce qui nous semble conforme à la règle. Ce mot a cependant diverses significations dans les diverses sciences. La conception est discutée dans ce travail, particulièrement au point de vue médical, mais aussi au point de vue artistique (littérature, musique, peinture). Il est démontré que dans la plupart des cas le mot *normal* représente l'usuel, mais qu'une notion de valeur y est également incluse.

Zusammenfassung.

Im täglichen Sprachgebrauch benützen wir das Wort „normal" und meinen damit etwas Gebräuchliches und uns richtig Erscheinendes. In den verschiedenen Wissenschaften hat das Wort sehr verschiedene Bedeutungen. In der vorliegenden Arbeit wird die Auffassung des Wortes vor allem vom medizinischen, aber auch vom künstlerischen Standpunkt (Literatur, Musik, Malerei) besprochen. Es wird gezeigt, daß in den meisten Auffassungen das Normale das Gebräuchliche ist, das Wort aber auch ein Werturteil einschließt. Deswegen kann man keine allgemein gültige Definition geben.

From the State Institute of Human Genetics and Race Biology, Uppsala, Sweden
(Head: Professor Gunnar Dahlberg, M. D., LL. D.)

Mathematics of the Genetics of Populations

by Gunnar Dahlberg

182 pages with 32 figures and 31 tables. 1947. Price sFr. 25.–

Out of the contents:

1. Division of characteristics from a hereditary viewpoint. 2. The conception of rac- and the laws of Mendel. 3. Different forms of inheritance. 4. Composition of populations in panmixia. 5. The effect of mutations on the composition of a population in panmixia. 6. The effect of selection on a population. 7. Selection and mutations. 8. The effect on inmarriage on a population. 9. Inmarriage and selection. 10. Assortae tive mating. 11. Assortative mating, inmarriage, selection, and mutations. 12. The importance of the isolate for the composition of populations. 13. Isolates and race. 14. Mutations, selection, and isolates. 15. Isolates and inmarriage. 16. Isolates, assortative mating, and selection. 17. General survey.

From the State Institute of Human Genetics and Race Biology, Uppsala, Sweden
(Head: Professor Gunnar Dahlberg, M. D., LL. D.)

Tooth Size and Occlusion in Twins

by Anders Lundström

206 pages with 29 figures. 1948. Price sFr. 16.–

Out of the contents:

Review of the Literature. Methods of Investigation. Statistical Methods Used. Cases Investigated. The Cases from a Representative Point of View. Loss of Teeth in Twins, and their Importance to the Material from a Representative Viewpoint. The Variation in Twins regarding Breadth of Teeth and Occlusion. Cases of Extreme Malocclusions. Significance of Genetic and Non-genetic Factors as regards the Tooth-Breadth and the Occlusion.

BASEL (Switzerland) S. KARGER NEW YORK